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GASTROSCOPY IN GASTRIC CARCINOMA

Especially in Its Early Diagnosis

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THE importance of gastroscopy in the early diagnosis of gastric carcinoma is disputed, although gastroscopists recognize its value in the differential diagnosis of benign and malignant lesions, and in the determination of operability. Gutzeit agrees that gastroscopy is of great value in the study of gastric carcinoma, but he does not believe that it will facilitate the early diagnosis. Moutier deems it impossible to diagnose an early gastric carcinoma either roentgenologically or gastroscopically, except in the antrum. Henning, who was skeptical, now states that gastroscopy would be important in the early diagnosis, were it widely performed. René Chevalier, who has made valuable contributions to this subject, contends that gastroscopy is superior to x-ray in some cases for the diagnosis of early carcinoma, and has published such cases. Benedict (2), who introduced gastroscopy in this country, has experienced the importance of the method in the early diagnosis. Schloss is hesitant in admitting the value of the method for this purpose. Schindler (35), as early as 1923, felt that gastroscopy would advance the early diagnosis of carcinoma, and presented 3 illustrative cases at that time.

We shall consider an "early" diagnosis of gastric carcinoma as one in which the lesion is very small, without clinically discernible metastases, invading so small an area that surgical removal may be undertaken hopefully. Other definitions have been used. Schindler (37, 38) has employed the term to mean a diagnosis which makes it possible to effect a "cure" of from 3 to 5 years after operation. The latter definition applies to the lesion of the size usually detected. However, with very small growths, the first definition is more practical.

From the Department of Medicine, University of Chicago.

Fig. 2. Case 1. Gastroscopic picture observed July 15, 1938. Antrum and pylorus are seen. The pylorus is rigid and not round. Behind two nodes on the greater curvature, a small (carcinomatous) ulcer is present.

Fig. 8. Case 2. Two gastroscopic views of a small carcinoma. In a, the greater curvature is visualized. A prominent wall with a superficial ulceration is seen. In b, the posterior wall is observed. The protruding tumor surface is much magnified.

Fig. 11. Case 3. Gastroscopic picture of a polypoid tumor lying in a completely atrophic mucosa.

Fig. 17. Case 6. Gastroscopic view of the anterior wall of the stomach, showing tremendous nodular infiltration and tumor-like protrusion of a fold. This picture is suggestive, but not conclusive, of carcinoma.

Fig. 19. Case 9. Gastroscopic picture of a type III carcinoma. At the right (3 o'clock), antrum and open pylorus are seen. The carcinomatous ulcer is limited toward the pylorus by a nodular wall. However, at 7 and 8 o'clock, no sharp limitation of the ulcer can be seen, evidence of infiltration. Between 10 and 1 o'clock, the overhanging posterior wall appears.

The importance of gastroscopy will be discussed in the early diagnosis of gastric carcinoma, in the differential diagnosis of benign and malignant lesions, in the determination of operability, and as a complement to x-ray. The essential question is: Can the early diagnosis be facilitated by gastroscopy? We believe and shall attempt to show that gastroscopy does facilitate early diagnosis, and that it is at times superior to all other methods.[1]

GASTROSCOPY IN THE EARLY DIAGNOSIS OF GASTRIC CARCINOMA

The results of treatment in early and advanced carcinomas must be differentiated. Cures, in the sense of 5 years or more respite from the disease, have been obtained in favorable cases (24). We therefore do not share the pessimism of those who believe surgery futile.

The following 3 cases[2] illustrate the developmental course and early diagnosis of gastric carcinoma.

CASE 1. No. 11283. A man aged 57 years, seen on May 18, 1938, had suffered from gnawing epigastric distress 2 hours after meals, for 1 year, associated with belching and impaired appetite. Food and alkali afforded relief. Beginning February, 1938, severe nausea occurred at 2 to 4 week intervals. In the 2 months prior to examination, epigastric distress was minimal, but there was a loss of 15 pounds. On ulcer management, instituted May 18, 1938, he was very comfortable.

Physical examination disclosed a well developed and nourished man with slight epigastric tenderness and moderate-sized hemorrhoids.

Laboratory examination revealed: hemoglobin, 85 per cent; red cell count, 4,600,000; white cell count, 8,000. Stools gave a 1 plus to 3 plus reaction to the benzidine test for occult blood. Gastric analysis, using histamine, revealed free acid (65) after 30 minutes.

Roentgen-ray examinations made on several occasions showed the following: May 24, fluoroscopy was negative. The films showed a constant rounded filling-in defect on the lesser curvature, just proximal to the pyloric canal. An ulcer crater was suspected. Rescreening was negative. June 1, a frank small lesion of the lesser curvature of the pyloric antrum was observed. The differential diagnosis could not be made between a small neoplasm with a central crater and a benign ulcer with considerable inflammation about it. June 29, a sharply circumscribed and outlined crater was seen, about 6 millimeters in diameter, proximal to the pylorus. About the crater, for perhaps 2 centimeters, a collar-like stiffness of the gastric wall was present. Due to the sharpness of the crater, the lesion was thought to be more likely benign, associated with considerable inflammatory swelling. The impression was that of a prepyloric ulcer with direct visualization of the crater, probably benign, but malignancy remained to be excluded. About the same impression was reached by another examiner on the same date.

July 16. A narrowing of the pyloric and prepyloric region was observed, with very little surrounding infiltration. The impression was that of a stenosing prepyloric ulcer (Fig. 1). Malignancy was doubted, but could not be ruled out absolutely.

Clinical impression. The relief of symptoms on ulcer therapy and the roentgen-ray findings were compatible with a benign lesion, but the clinician was unable to make such a diagnosis in the face of a positive gastroscopic diagnosis of carcinoma.

Three gastroscopic examinations were performed, June 8, June 22, and July 15 (Fig. 2, frontispiece). At the first examination, the visualization of the distorted pylorus, which was overlapped by two protruding nodes, strongly suggested a malignancy. Operation was therefore recommended. Severe hypertrophic gastritic changes of the lower part of the body were also observed. At the second and third examinations, essentially the same picture was found, but the hypertrophic gastritic changes had decreased in extent, and the mucosa of the greater curvature of the antrum appeared gray, thin, and atrophic. The protocol of the final examination read, "A most distinctly pathological pylorus was visualized. Its ring was stiff, irregular in shape, and definitely infiltrated. One large node was protruding from the posterior wall, and another between the anterior wall and greater curvature. Between this latter node and the pyloric ring, an irregular, dirty gray, small ulceration was seen. The mucosa adjacent to the pylorus seemed to bulge inward into the antrum. The mucosa of the greater curvature of the antrum was smooth, thin, and grayish (atrophic gastritis). Large peristaltic waves closed the antrum with stellate formation, at a distance approximately 3 centimeters from the pylorus (pathological type III pyloric action). Impression: Ulcerative and infiltrative carcinoma of the pylorus, with atrophic gastritis. There is no room for differential diagnosis. The area involved is still small. Delaying surgery is no longer justified."

On July 16 operation was performed. A small lesion was felt in the pyloric region, which was thought to be a benign ulcer. Partial gastrectomy was done. Recovery was uneventful.

Pathological examination. In the center of the specimen (Fig. 3) was a small, shallow ulcer, 0.5 centimeter in diameter, and 1 to 1.5 millimeters in

[1] All examinations were performed with the Wolf-Schindler flexible gastroscope.

[2] Unless otherwise indicated, all cases were referred by Dr. W. L. Palmer, chief of the gastro-intestinal clinic, University of Chicago Clinics; roentgen examinations were performed by the department of roentgenology (Dr. Hodges, Dr. Templeton); and operations by the department of surgery. We are indebted to them for their close cooperation.

depth. The margins were sharp, punched-out, and irregular in outline. Some thickening was felt at the ulcer site. The lesion appeared benign grossly. Microscopically (Figs. 4, 5, 6), an unusually small carcinomatous growth was seen. The tumor area is 8 millimeters wide and 0.5 millimeter deep generally, and composes the floor of the ulcer. The tumor cells partly cover the surface of the long Brunner glands, and partly reach the muscularis mucosæ. They form solid nests with a scant stroma. At only one small area, they penetrate the muscularis mucosæ to a depth of 2 millimeters. Here they form adenomatous tubules, and there is an extensive inflammatory reaction which consists of lymphocytes, leucocytes, eosinophiles, and plasma cells. The adjacent mucosa shows considerable reduction in the amount of glands, metaplasia of the glandular epithelium with formation of goblet cells, tremendous interstitial infiltration, and enlargement of the lymph follicles. Diagnosis: (1) Carcinoma, partly simplex and partly adenomatous, of minimal size; (2) extensive atrophic gastritis.

The gastroscopic appearance of the lesion was so definitely that of a carcinoma that no other lesions were considered in a differential diagnosis. The roentgen findings and clinical course were entirely compatible with a benign lesion. At operation and after examination of the gross specimen, a benign lesion was considered more likely. The accuracy of the gastroscopic diagnosis was confirmed only by the microscopic examination. Microscopically, it is evident that the infiltration surrounding the ulcer, as seen in roentgen examination, was not tumorous, but inflammatory, and that the nodes seen gastroscopically were also inflammatory rather than carcinomatous. Two questions obviously present themselves: (1) Why was it possible to make a gastroscopic diagnosis that could only be corroborated microscopically, and not by gross examination of the specimen? (2) How could a malignant lesion of such unusually small extent (8 by 2 millimeters) be diagnosed?

1. It has often been contended that the gastroscopic appearance of a lesion is occasionally more accurate than the surgical and pathological observations of the gross specimen, and second only to the microscopic examination. Benedict has had this experience also. The reason is the high relief pattern and the brilliantly colorful appearance of the living tissue in the gastroscopic picture, due to the presence of circulating blood. In Case 1, here presented, the irregular, dirty appearance of the small ulcer seen at the pyloric ring was not characteristic of a benign ulcer. However, still another factor contributed to the correct diagnosis. It is well known that benign ulcers at the pylorus can rarely, if ever, be observed gastroscopically, because scar formation or adhesions displace the pylorus upward, out of the gastroscopic visual field. Therefore, experience has taught that if a pyloric ulcer can be seen gastroscopically, almost invariably it is carcinomatous. This rule has been applied to the presented case, and again found correct.

2. The second question asks the means for recognizing so small a lesion. It has been emphasized repeatedly that early gastric carcinomas will be detected only when we examine thoroughly patients with slight gastric distress, or none at all, but only some weight loss and lack of appetite. The patient in Case 1 was treated according to these requirements. His abdominal distress was minimal at the time of examination, but he sought medical advice because of his weight loss. The thorough examination undertaken because of this complaint, including roentgen-relief studies and gastroscopy, led to correct diagnosis and therapy.

It appears very unlikely that a small carcinoma, 8 by 2 millimeters, was present at the onset of illness, one year before its discovery. The patient's symptoms at that time may have been due to the presence of chronic atrophic gastritis, observed gastroscopically, which often precedes the development of carcinoma. This important subject will be discussed later. If a benign ulcer had been present originally, it probably would have been impossible to see the pylorus gastroscopically, owing to consequent displacement out of the visual field. It seems to us very doubtful whether any of the patient's symptoms were due to the carcinoma itself, since the tumor was of minimal size, there was no food retention, and considering that chronic atrophic gastritis frequently may cause severe weight loss, anorexia, and epigastric distress.

We are therefore inclined to believe that the symptoms were gastritic in origin, and led to the careful roentgen and gastroscopic ex-

aminations, which, in turn, permitted the *incidental* discovery of the small carcinoma. In this respect, the case should be compared to Case 2, in which the incidental discovery of the lesion is even less questionable.

CASE 2. No. 200796. A man aged 59 years, seen June 24, 1938, had suffered progressively increasing weakness with ascending numbness in the lower extremities for 3 years. At the onset of symptoms, a diagnosis had been made of pernicious anemia with combined cord degeneration. Liver extract had been prescribed, but irregularly taken. In April, 1938, he was observed in another hospital, and treated with liver extract and transfusions. Roentgen studies were made in the course of a routine examination, and a "filling defect" seen in the *prepyloric area*, suggesting a carcinoma (Fig. 7). (Examination of these films here indicated the apparent defect was produced by pressure of the spine, since mucosal folds were present at this site in the relief films). There was a loss of 15 pounds in the past 2 months, and increasing constipation, but the appetite remained good. In the last week, he was unable to walk, owing to neurological changes. No definite gastric symptoms were present.

Physical examination disclosed an obese, pale male, with neurological signs of subacute, combined cord degeneration.

Laboratory examination revealed: hemoglobin, 78 per cent; red cell count, 3,400,000; with blood smear characteristic of pernicious anemia. Wassermann and Kahn tests were negative. Stools gave a 4 plus reaction for occult blood. Gastric analysis revealed a histamine-refractory anacidity.

Roentgen-ray and gastroscopic examinations gave the following results: Roentgenogram on June 27 showed that the stomach and duodenum were normal. In view of the outside x-ray diagnosis of carcinoma, gastroscopy was advised.

Gastroscopic examination was made on August 1 (Fig. 8, A and B, frontispiece). The paralysis of the lower extremities caused some difficulty, but the examination was complete. The pylorus was observed in full activity. Although the antrum mucosa was slightly swollen, no tumor was seen. A gray atrophic patch was seen above the muscular sphincter antri. When the objective was turned toward the posterior wall of the mid-portion of the stomach, in the course of the routine examination, a prominent tumor appeared in the field. It was limited by a wall, the edge of which was necrotic. There was no demarcation toward the posterior wall, the tumor passing gradually into the dark red neighboring mucosa at this point. Toward the greater curvature, separated from the tumor mass by a bridge of normal mucosa, a small polypoid tumor was seen. A diagnosis was made of type III carcinoma of the mid-portion of the posterior wall near the greater curvature with atrophic gastritis.

A repeat roentgenogram was made on August 2, in view of the gastroscopic diagnosis of carcinoma. The findings were again negative. However, the patient was difficult to examine because of his obese abdomen and inability to use his legs.

Operation was performed on August 11. A small carcinoma was found in the mid-portion of the stomach, on the posterior wall close to the greater curvature. There was no evidence of metastases. A subtotal gastrectomy was performed. The patient expired 3 days later from a pulmonary embolus.

Pathological examination. The tumor (Fig. 9) is 4 by 1.7 centimeters, lying on the posterior wall, close to the greater curvature. There is a limiting wall at the greater curvature side. At the upper portion toward the posterior wall, there is a diffuse infiltration without sharp demarcation. A shallow ulceration, 1.2 centimeters in diameter, is present. Microscopically (Fig. 10), an adenocarcinoma is seen penetrating into the submucosa, the stroma of which contains many cells. The depth of the surrounding mucosa and the number of glands are reduced. There is a tremendous cellular infiltration, consisting of lymphocytes, plasma cells, and eosinophiles. At some places metaplasia of the epithelium is present (atrophic gastritis). The lymph follicles are increased in size and number.

In this case, an early gastric carcinoma was diagnosed because a patient with pernicious anemia was examined gastroscopically in spite of the negative roentgen observation. There were no symptoms definitely referable to the stomach. However, the roentgenologist advised gastroscopy despite his normal findings, which shows the need for close co-operation between roentgenologist and gastroscopist. Had this patient been examined earlier gastroscopically, it is quite probable that a smaller lesion would have been detected.

The procedure of the outside hospital in making a complete examination with x-ray studies was commendatory, although a diagnosis of pyloric tumor was incorrectly made due to faulty interpretation. Careful roentgen re-examination failed to reveal a tumor. The value of gastric roentgen relief studies for the early diagnosis of carcinoma should not be underrated because of the presentation of this case. However, there are cases in which gastroscopy is superior to careful relief technique. Four similar cases have been reported by Katsch. Benedict (2), and Moersch and Snell mention this occurrence.

This case and the one following demonstrate well the value of periodic examinations for the early recognition of gastric carcinoma in pa-

Fig. 1. Case 1. Roentgenogram, July 16, 1938, showing a "fleck" suggestive of pyloric ulcer.

tients with atrophic gastritis. This subject is further discussed later. There is some evidence of an increasing frequency of gastric lesions in the course of pernicious anemia (44). Chronic atrophic gastritis is the predisposing factor for the development of gastric polyps and carcinoma, according to Konjetzny (20), and others. If this is true, Hurst (14) suggests an increase in the incidence of gastric carcinoma in pernicious anemia patients is to be expected, as a result of the more adequate treatment with extension of the life expectancy. Benedict (3) mentions the incidental discovery of 2 cases of gastric carcinoma, in the gastroscopic examination of several cases of deficiency disease with atrophic gastritis (one a pernicious anemia, the other a Plummer-Vinson syndrome), which were confirmed by x-ray and resected.

CASE 3. No. 188610. An attorney aged 58 years, seen February 20, 1938, complained of indefinite gastro-intestinal distress for 20 years. In 1928, gastric analysis revealed free acid. But during the last 10 years, several examinations showed anacidity after histamine. In the last 5 years, there was a progressive state of weakness and fatigue, developing into marked exhaustion on little effort. As a result, a formerly very active man was compelled to curtail his activities drastically. In the past 8 months, more definite gastric symptoms appeared, principally epigastric pains, aversion to food, with a loss of several pounds.

Ulcer diet and rest were initiated. This relieved the distress but not the weakness. In the last month, the pain increased despite treatment. Repeated

Fig. 3. Case 1. Drawing of the resected specimen. The pyloric ulcer was so shallow that it was obscured in the photograph. In the drawing, it appears deeper than actually, for the purpose of demonstration.

roentgen-ray examinations were made over a period of 10 years. Although no definite lesion was found, the tentative diagnosis of gastric ulcer was made. For the last 3 years, a very gradual drawing in of the greater curvature opposite the angulus was observed, interpreted as a spasm. Review of all films at the time of examination showed a filling defect on the greater curvature of the lower pole of the stomach, the first sign of which had appeared 3 years before, and slowly became more marked.

Laboratory examination revealed: Hemoglobin, 105 per cent; red cell count, 5,500,000; white cell count 8,000; sedimentation rate, moderately increased; stools, occasionally 1 plus.

Gastroscopy carried out on February 20 (Fig. 11, frontispiece), revealed a polypoid, nodular, rather sharply defined tumor of the greater curvature of the antrum, extending toward the lower pole of the stomach. It was not ulcerated. The nodes of its surface were of varied size. There was a complete atrophy of the gastric mucosa from the cardia to the pylorus. The gastroscopic diagnosis was that of a polypoid carcinoma (type I, see below) of the greater curvature of the antrum, which had slowly developed on the soil of a severe atrophic gastritis.

At operation March 18, the tumor was found at the area described gastroscopically, and a resection was performed.

Pathological examination. A polypoid tumor was present, 6 by 5 by 1.5 centimeters in diameter, and not ulcerated (Figs. 12, 13, 14). Microscopically, the tumor showed early malignant degeneration of a gastric polyp, with severe atrophic gastritis throughout the entire operative specimen.

Fig. 4. Case 1. Photomicrograph of a section made through the carcinomatous ulcer shown in Figure 3. The ulcer floor consists of a thin layer of carcinomatous tissue, the average thickness of which is 0.5 millimeter. At the site indicated by an arrow, the growth has penetrated through the muscularis mucosæ to a depth of 2 millimeters. The width of the ulcer surface is 8 millimeters.

Reviewing the case history, there can be little doubt that the development of a polypoid carcinomatous tumor was preceded by a chronic atrophic gastritis of at least 10, but probably 20, years' duration. The histamine-refractory anacidity over a period of 10 years was a manifestation of atrophic gastritis. Thus this case supports the theory that carcinoma frequently develops on the soil of chronic atrophic gastritis, a sequence of events which very likely occurred in Cases 1 and 2. The general symptoms of the patient, especially his weakness and incapacity to work, are prominent manifestations of atrophic gastritis. It is questionable whether the very small filling defect present 3 years previously was evidence of a malignant tumor. It is more logical to assume that at first a very small benign tumor developed on an atrophic gastritis, which only recently degenerated into malignancy. Miller, Eliason, and Wright (25) reported carcinomatous degeneration in 8 of 23 cases of gastric polyps. An atrophic gastritis was probably the precursor in all, as Miller later recognized (26), particularly evident in their sixth case.

In Case 1, the symptoms leading to gastroscopic examination were due either partly to the presence of an extremely small pyloric carcinoma (weight loss, perhaps), or entirely to the concomitant atrophic gastritis. In Cases 2 and 3, the relationship between atrophic gastritis and tumor formation is much more obvious, and suggests important conclusions as regards a practical program for the fight against gastric carcinoma.

The histopathological and clinical studies of Saltzman, Konjetzny (20, 21, 22, 23), and Staemmler indicate a transition from chronic gastritis to carcinoma. Faber concurs with these pathological observations. Clinically, Hurst (13, 15, 16) has argued strongly for this concept. Miller (26), Bloomfield, Usland, Katsch, Kapp, Tuomikoski, and others now agree that in most cases carcinoma develops on the seat of a chronic gastritis.

In 1922, Schindler (33) urged the necessity for examination of patients with minor gastric distress to achieve early diagnosis of malignancy and felt that gastroscopy would be important in this respect. In 1933 (36), he was perhaps the first to advocate periodic examination of patients with precancerous conditions (atrophic gastritis and benign tumors). He maintained that atrophic gastritis can best be recognized gastroscopically, and that gastroscopy permits the diagnosis of small tumors better than roentgen-relief technique in some cases.

Katsch's views on the subject of early diagnosis of gastric carcinoma are very important. He believes that the stage of relative latency, with minor uncharacteristic symptoms, is the time for early diagnosis. Although he holds x-ray the chief means for this purpose, he recognizes the method is not infallible even in the best of hands, and gastroscopy superior in some cases. He therefore urges the wider use of gastroscopy. Since gastritis is the soil for the growth of carcinoma, he feels that the resources and efforts applied to the fight against gastric carcinoma should be used for research on gastritis, and careful observation of patients suffering from gastritis, even when few or no symptoms are present. Similarly, Miller (26) states that to prevent the development of gastritis and the diseases for which it seems responsible, much experimental and clinical investigation is necessary on gastritis. Alessandrini advises the use of gastroscopy as a means of recognizing the precancerous con-

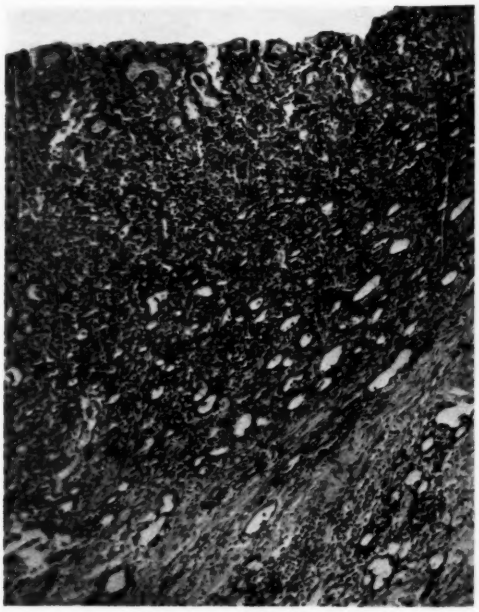


Fig. 5. Case 1. Photomicrograph of a section made through the carcinomatous growth shown in Figure 4, with higher magnification. ×85.

Fig. 6. Case 1. Photomicrograph of a section made through the gastric wall adjacent to the carcinomatous ulcer shown in Figures 1 to 5. Severe atrophic gastritis. The gastric glands have almost disappeared. Metaplasia of the surface epithelium into goblet cells. Interstitial infiltration.

dition of chronic gastritis. Presenting 2 cases in which gastric carcinoma developed following chronic gastritis, Comfort and Butsch state that if it is accepted that chronic gastritis is the soil in which carcinoma develops in a large percentage of cases, it will greatly affect the methods used in the prophylaxis and early diagnosis of carcinoma; and that gastroscopy may become most important for this purpose, since a growth may be in its precarcinomatous state or too small for demonstration by x-ray.

Kapp analyzed 120 cases of gastric carcinoma as to the early symptomatology, with startling results. Gastritic symptoms were present at least 5 years before the diagnosis of carcinoma was made in 12 of 66 cases of pyloric carcinoma, and in 24 of 29 cases of body carcinoma. In another series of 157 cases diagnosed clinically as gastritis, 21, or 13.4 per cent, developed carcinoma in 5 years or later, which incidence is about three times that of gastric carcinoma in general. Kapp concludes from his statistical study that to effect an early diagnosis, cases of chronic gastritis should be given more attention, and that periodic gastroscopic examinations should be done.

Usland made similar observations in a study of 94 patients operated upon for gastric carcinoma, and 120 with diagnosis of gastritis. In the 94 cases with operations, 26, or nearly 28 per cent, had suffered from dyspeptic symptoms more than 5 years prior to clinical manifestations of carcinoma, such symptoms having been interpreted as due to chronic gastritis. In 120 patients over 30 years of age, who, when first seen during 1922 to 1929 had suffered from symptoms of chronic gastritis for at least 2 years, he found that 18, or 15 per cent, had developed gastric carcinoma in the course of years.

These statistics of Kapp and Usland coincide and are very significant. It is hoped that in the future such studies will be based on the more accurate gastroscopic diagnosis of gastritis. There is strong evidence that the diagnosis of early carcinomas may be made by finding them *incidentally* in the re-examination of patients with precancerous conditions. *If we wait until the tumor itself produces symptoms, we cannot hope to diagnose a carcinoma of minimal size.*

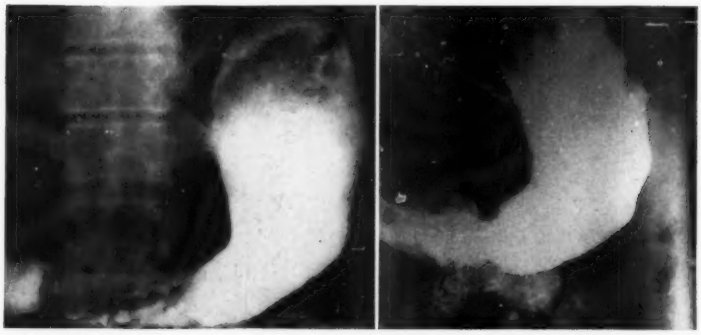


Fig. 7. Case 2. Two roentgenograms made at different institutions. The apparent prepyloric filling defect shown in a, left, is artificially produced by the pressure of the spine. The actual tumor, lying much higher, on the posterior wall of the mid-portion near the greater curvature, was not demonstrated by either examination.

The 3 cases of early diagnosis of gastric carcinoma which have been presented suggest the following conclusions:

1. Any patient in the carcinoma age (over 35) suffering from unexplained minor epigastric distress should be examined by the roentgen-relief method and gastroscopically.

2. Precancerous conditions, such as chronic atrophic gastritis and benign gastric tumor, should be diagnosed by gastroscoping every patient suffering from mild gastric symptoms, or the general symptoms of atrophic gastritis (weakness, loss of weight, etc.).

3. When these diseases are found, periodic roentgen and gastroscopic examinations should be made. Only then can small carcinomas be discovered.

GASTROSCOPY IN THE DIFFERENTIAL DIAGNOSIS OF BENIGN GASTRIC ULCER AND MALIGNANCY

The differential diagnosis of benign and malignant gastric lesions can usually be made gastroscopically. It has occurred even in such cases in which examination of the gross specimen gave an uncertain diagnosis. This statement puzzles the pathologist, but the reason, as mentioned in the discussion of Case 1, is the presence of circulating blood in the living tissues studied gastroscopically. A roentgen diagnosis of carcinoma has been made occasionally when gastroscopy reported a benign lesion. In most of these instances, microscopic examination confirmed the gastroscopic observation. Gutzeit and Teitge, Schindler (37, 38), and Benedict (2) have presented striking cases of this type. The following 3 cases, however, demonstrate roentgenologically benign ulcers in which the gastroscopic diagnosis differed.[1]

CASE 4. No. 130055. This case has been described elsewhere (38), and shall be mentioned briefly here.

A man aged 71 years complained of gnawing epigastric distress after meals for 3 years, with relief by food and alkali. The gastric contents, after histamine, revealed free acid (28) after 30 minutes. Stools gave a negative to 4 plus reaction for occult blood. Seven roentgen examinations were performed from June 17 to October 31, 1935, and the impression was that of a large penetrating ulcer of the cardiac end of the lesser curvature. The third and fourth examinations showed the crater becoming smaller, during ulcer management (Fig. 15). The first gastroscopy was done June 22, 1935, shortly after the first x-ray study, and a diagnosis of an ulcer-like carcinoma of the lesser curvature was made because of a grayish ridge-like prominence arising from the large crater, which was filled with blood coagula.

A second examination made on July 8 confirmed the diagnosis of carcinoma, since the ulcer was situated on an elevated area and one part of its edge was not sharply defined. Since the lesion was limited toward the cardia and progressive toward the pylorus, radical operation appeared possible. Surgery was performed when x-ray concurred in the diagnosis of carcinoma, and an ulcerating carcinoma of the lesser curvature was resected (November 4).

[1] The histological aspects of these 3 cases are to be reported by W. L. Palmer and J. L. Ferry.

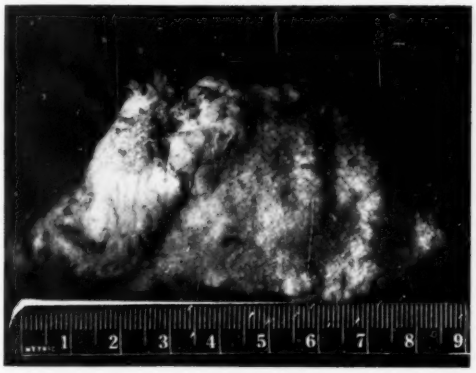


Fig. 9. Case 2. A portion of the resected specimen, showing a small ulcerated carcinoma.

This case demonstrates well the value of gastroscopy in differentiating between a benign and malignant lesion of the stomach. The history and roentgenogram suggested a benign lesion. The gastroscopic diagnosis, however, was definite at the first examination. The fact that the niche became smaller in roentgen examination is important. This phenomenon also occurred in Cases 5 and 6.

CASE 5. No. 164708. A man aged 65 years, seen November 30, 1936, suffered from epigastric pain unrelated to meals for 1 year, with a loss of 20 pounds. Ulcer management for the next year gave partial relief. In September, 1938, hematemesis occurred, with increase in severity of the pain. Physical examination was non-contributory. Laboratory examination showed a secondary anemia, occult blood in the stools, and free acid in the gastric content (17).

Roentgen-ray examination made on December 21, 1936 showed a large questionable ulcer on the posterior wall near the cardia. Re-examination was advised. (The first gastroscopy, December 23, 1936, suggested a malignancy.)

On January 27, 1937, a gastric ulcer was observed on the posterior-superior wall, which had decreased slightly in size since the previous examination. On April 13 the ulcer crater near the cardia appeared much larger. The possibility of a neoplasm was not ruled out. On October 23, one or both of the irregular puddles of barium seen in the floor of the gastric shelf were interpreted as ulcer craters.

The first gastroscopic examination, made December 23, 1936, was difficult, because the visual field was partially obscured by fresh blood. On the posterior wall, a very large and deep ulcer was seen, with grayish white floor. Parts of the edge were covered by blood. The inferior ulcer edge seemed

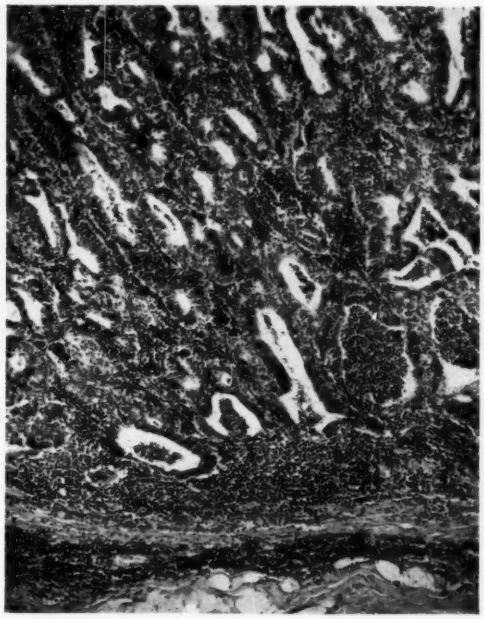


Fig. 10. Case 2. Photomicrograph of a section made through the carcinoma seen in Figures 8, frontispiece, and 9. Adenocarcinoma. ×70.

rather sharp, but superiorly the edge appeared to blend with the surrounding mucosa. The impression was that of a large, deep ulcer of the upper posterior wall, more likely a malignancy. But re-examination was advised before a definite diagnosis was made, owing to the interfering hemorrhage present.

Further roentgen examinations and the clinical course were more suggestive of a benign ulcer, especially since the ulcer niche at one time appeared smaller. For these reasons, and because of an intervening urological condition, the patient was not referred for gastroscopy until 10 months later (October 20, 1937). This examination was impossible, however, because of an organic obstruction at the cardia.

At operation, November 9, 1937, an inoperable carcinoma of the stomach was found, high on the posterior surface of the stomach, encroaching on the lesser curvature and involving the esophagus.

Gastroscopy suggested a malignancy in this case almost 1 year before operation, although a definite diagnosis was not permitted because of a partially obscuring hemorrhage. The gastroscopic observation of a partial blending of the ulcer edge with the surrounding mucosa could not be reconciled with a diagnosis of

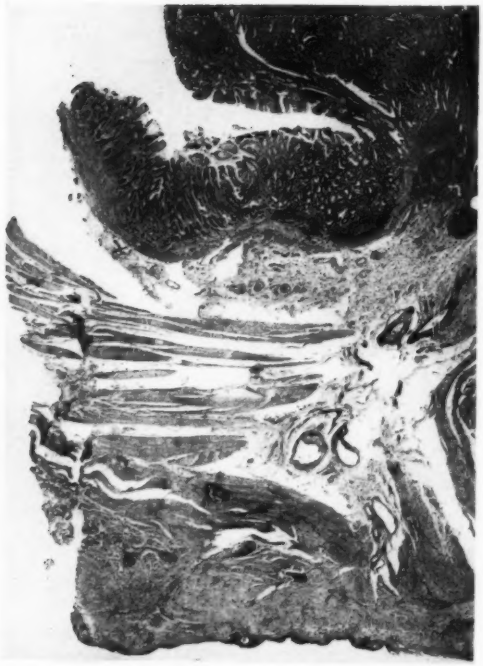


Fig. 12. Case 3. Photomicrograph of a section through an edge of tumor seen in Figure 11, frontispiece, showing the gradual transition of atrophic gastric mucosa into tumor tissue. The completely atrophic gastric mucosa, present on the left side, undergoes malformation and proliferation in the center of the picture. The proliferation develops into tumor formation at the right of the picture.

benign ulcer. Here, again, the niche of a malignant ulcer was seen to diminish in size during roentgen study.

Case 6, No. 162012. A man aged 54 years, seen October 16, 1936, complained of epigastric distress radiating to the back, 1 to 2 hours after meals, for 2 months. Milk and alkali gave relief. Hematemesis of severe degree had occurred three times in the previous year. Weight loss was considerable.

Physical examination disclosed marked pallor and weakness.

Laboratory examination, October 16, 1936 revealed: hemoglobin, 20 per cent; red cell count, 2,400,000; stools occasionally positive for occult blood. Gastric analysis revealed free acid (105) 50 minutes after histamine. In January, 1937, hemoglobin was 95 per cent; red cell count 4,700,000; stools occasionally positive for occult blood. In September, 1937, hemoglobin was 65 per cent; red cell count, 4,000,000. One stool of many showed occult blood. Gastric contents contained free acid (30) fasting, and (115) 40 minutes after histamine injection.

Twelve roentgen-ray examinations were performed from October, 1936, to September, 1937 (Fig. 16), observing the course of a large penetrating ulcer high on the lesser curvature, and of a second ulcer developing in the antrum during the course of therapy for the higher ulcer. A marked gastritis was diagnosed, surrounding the lesser curvature ulcer. The lesions were believed to be benign ulcers because of their rapid change in size. The upper ulcer crater was large and penetrating in October, 1936, but appeared to be healing rapidly on November 10, 1936. The prepyloric ulcer observed on January 19, 1937, had disappeared on February 3, 1937. The upper ulcer had increased in size in April, 1937. On September 10, 1937, again both ulcers were seen. Marked enlargement of the rugæ was noted several times, and the possibility of a malignant infiltration was sometimes considered.

In nine gastroscopic examinations from October 28, 1936, to September 11, 1937, an ulcer was never seen, but a tremendous infiltration of the entire gastric wall with loss of plasticity was observed, of a type never accompanying benign ulcer (Fig. 17, frontispiece). Stiff, elevated folds and nodes were prominent, which suggested either infiltration by tumor, or by an unusually severe and rare form of gastritis. Other rare infiltrative lesions were also considered, such as lymphoblastoma and Hodgkin's disease. A definite diagnosis could not be made. Finally, a narrowing of the cardia was observed and gastroscopies were discontinued.

Clinical course. The clinical impression of gastric ulcer was supported by the response to ulcer treatment and the roentgen findings. The patient remained well controlled until August, 1937, when mild epigastric distress, weakness, loss of weight and appetite recurred. Abdominal ascites and a firm mass within a left inguinal hernia were observed September 2, 1937. Exploration of the hernial sac and biopsy of the thickened peritoneum within, September 20, 1937, showed carcinoma, believed metastatic from a gastric colloid carcinoma. The patient grew progressively weaker and expired in February, 1938.

Autopsy was performed in February, 1938. A diffusely infiltrating carcinoma of the entire stomach was found with widespread peritoneal metastases. Inspection of the mucosal surface, however, was misleading, since it appeared rather smooth and flat. An ulcer was present on the lesser curvature, with fixation to the pancreas. Microscopically (Fig. 18), the entire stomach showed diffuse infiltration by solid, and particularly colloid-forming, carcinomatous nests. The surface of the ulcer was lined by tumor tissue. Its base showed extensive fibrosis.

It was difficult gastroscopically to differentiate definitely between an unusually severe hypertrophic gastritis and other infiltrative

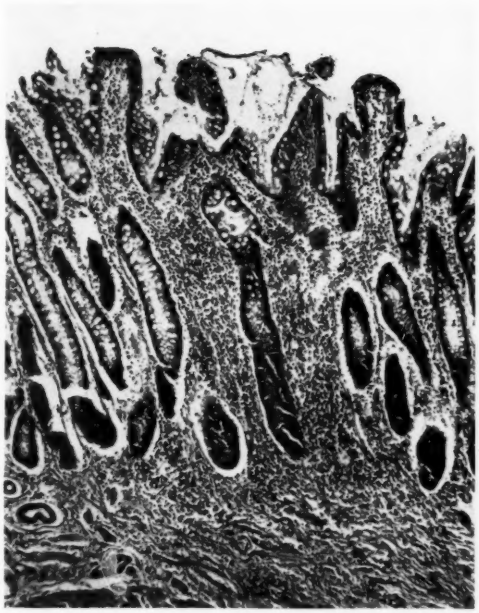


Fig. 13. Case 3. Photomicrograph showing the area of atrophic gastritis, present in Figure 12, under greater magnification. Almost complete metaplasia of the epithelium into intestinal epithelium, decrease in the number of glands, and interstitial cellular infiltration. ×55.

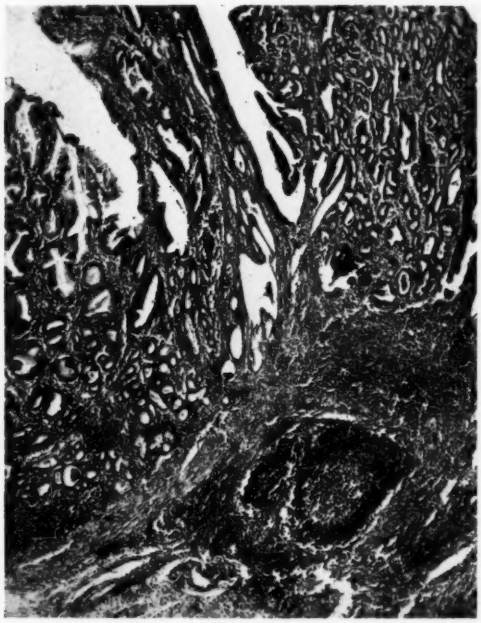


Fig. 14. Case 3. A higher powered view of the edge of the tumor seen in Figure 12. At the left, metaplastic gastric mucosa can be seen. In the center and to the right of this illustration, formation of regular adenomatous tubules into tumor are observed.

lesions, including carcinoma. However, a benign ulcer was excluded. We have never seen such extensive infiltrative changes accompanying a benign ulcer. The patient was well controlled for 8 months following the first examination, and roentgen studies tended to confirm the clinical diagnosis of a benign ulcer. Gastroscopically the ulcer was not visualized, but the picture seen at the initial examination was in accord with the autopsy findings of a tremendous diffuse infiltrative process of the entire gastric wall. The failure to see the ulcer may be attributed to an overlapping infiltrated fold, or a location in the gastroscopic "blind strip" of the posterior wall.

The difficulty in differential diagnosis between severe diffuse hypertrophic gastritis and other diffusely infiltrating processes, such as carcinoma, lymphoblastoma, Hodgkin's disease, syphilis, has been experienced on several occasions by Schindler, in 10 of 2,000 patients (38), Moutier (28), and Benedict (2, 3). However, the diffusely infiltrating carcinoma is by far the most frequent of such lesions, and must be strongly considered until definitely ruled out.

It might be argued here that a benign ulcer underwent malignant degeneration. However, the diffuse infiltrative changes were observed early gastroscopically (16 months before death), retrospective evidence of the presence of carcinoma at that time. This case illustrates again the danger of utilizing the roentgen diminution in size of the niche as an argument against malignancy.

Cases 4 and 5 demonstrate that although an ulcer may appear benign clinically and by roentgen-ray study (decrease in size of the niche, etc.), gastroscopy may enable one to make a positive diagnosis of malignancy at the initial examination. In our experience,

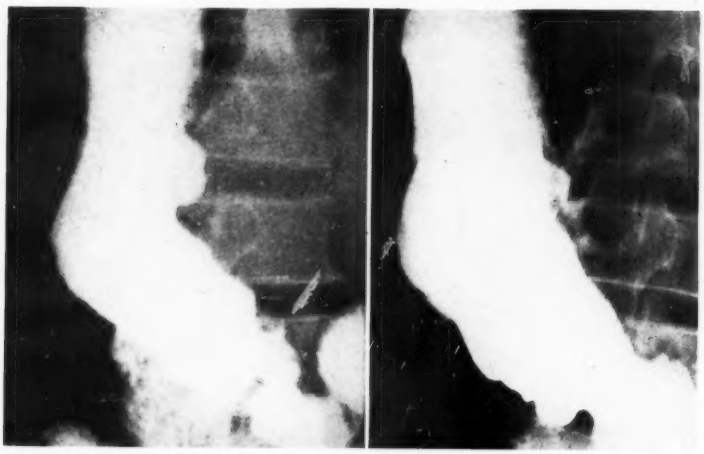


Fig. 15. Case 4. Roentgenograms made in June and July, 1935, respectively, of a malignant ulcer. Because of the decrease in size of the niche, a benign ulcer was assumed. The gastroscopic picture and the pathologic examination revealed a carcinoma.

the finding of such an extensive infiltrative process as in Case 6 warrants a presumptive diagnosis of malignancy. It is obviously wrong to assume that a niche is produced by a benign ulcer because it becomes shallower during roentgen-ray observation of a few weeks. Bloomfield has described similar cases. Much valuable time may be lost by relying on this therapeutic test. Secondly, without gastroscopic observation in these 3 cases, the development of carcinoma from benign ulcer might be assumed because of the long history, clinical picture, and roentgen-ray findings. Gastroscopy, however, revealed the presence, or evidence of, carcinoma at the earliest stage of observation. It is conceivable that similar cases have been described in the literature as examples of carcinoma developing from ulcer. Early gastroscopy in these cases, had this method of investigation been used, might have altered this belief.

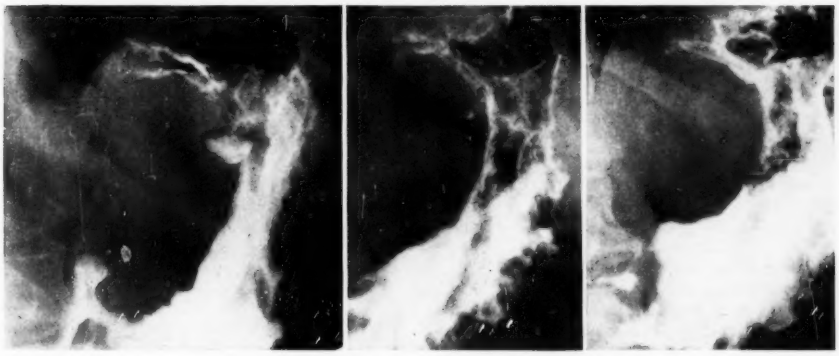
GASTROSCOPY IN DETERMINATION OF OPERABILITY

Most gastroscopists agree that the method is important in the determination of operability, site, and extent of gastric carcinoma. Exploratory laparotomy for determination of operability may be avoided in most cases by gastroscopy, although other factors may also determine this (general condition of the patient, presence of metastases). We believe gastroscopy superior to roentgen-ray examination in this respect. No surgeon considers exploratory operation satisfactory when the condition proves inoperable. It should be done only in those relatively few cases in which the operability is not definitely determined gastroscopically. This should lower the surgical mortality and dispel the unfortunately common belief in the futility of surgical treatment of gastric carcinoma.

We have found Borrmann's classification of gastric carcinoma, according to the macroscopic appearance, to be the most practical in rendering a prognosis. This classification corresponds completely with the gastroscopic observations:

Type I, polypoid carcinoma. This type is sharply limited, operable, and gives an excellent prognosis. It occurred in 2.9 per cent of the carcinomas observed gastroscopically by Schindler.

Type II, non-infiltrating carcinomatous ulcer. This lesion is surrounded by a sharply limited wall, is common, and gives a good prognosis. It was found in 17.6 per cent of carcinomas.



a b c

Fig. 16. Case 6. Roentgenograms of a malignant ulcer, the niche disappearing during observation. a, made October 7, 1936, shows a large niche at the upper portion of the lesser curvature. In b, made June 28, 1937, the niche has become very small. In c, made August 13, 1937, the niche has disappeared.

Type III, infiltrative carcinomatous ulcer. This tumor is only partially surrounded by a limiting wall. If operable, the prognosis is still doubtful. It occurred in 16.3 per cent of carcinomas.

Type IV, diffuse infiltrating carcinoma, which may be ulcerated but little. It almost always gives a bad prognosis, and even if resectible, goes on to early recurrence and metastases. It occurred in 63.2 per cent of carcinomas.

The usual criteria of operability have been whether the tumor can be excised *in toto*, the resection being done in non-cancerous tissue, and there is no evidence of widespread metastases. The surgeon has no other criteria during the operation, if there is no preceding gastroscopic examination to distinguish the type of tumor present, according to the Borrman classification. In our experience, as judged by the end-results, the type has played an important part in the ultimate course. Gastroscopy is the best method for determining the type of carcinoma before operation, thus indicating the prognosis. In cases of minimal-sized carcinomas, the prognosis of this classification should be disregarded for practical purposes. It is to be hoped that carcinomas of very small size will give a good prognosis regardless of their type. Carcinomas involving the cardia have not been included in the types described, since the surgical approach is relatively recent, and there has been insufficient time to determine the end-results.

Even with the usual criteria of operability, gastroscopy is of value, as will be shown in the cases following.

Case 7. No. 640-887, Cook County Hospital.[1] A man aged 68 years, seen July 1, 1937, complained of gnawing epigastric distress for 8 months, with a loss of 21 pounds in 1 year. Physical examination revealed a poorly nourished male, with slight tenderness surrounding the umbilicus. Gastric contents contained no free acid after an Ewald meal.

Fig. 18. Case 6. Photomicrograph of a section made through a carcinomatous ulcer. Not only the entire ulcer floor, but also the gastric mucosa is infiltrated with carcinoma.

[1] We are grateful to Dr. M. Hubeny for his co-operation.

Roentgen-ray examination, July 8, 1937, revealed a constant irregularity along the greater curvature of the pars media and pars pylorica, which was apparently intrinsic and compatible with a diagnosis of carcinoma.

Gastroscopy, July 5, disclosed a type II sharply demarcated carcinoma in the antrum, its upper margin lying at the level of the angulus.

Operation was done July 10. A large ulcerated lesion was found, with the infiltration extending upward throughout the entire wall of the stomach, almost up to the cardia. A very high subtotal gastrectomy was performed.

Pathological examination. The senior author thought the gross specimen showed almost complete carcinomatous involvement. In the region of the lesser curvature, near the pyloric end, and extending anteriorly, was a firm mass, 6½ by 6 centimeters. The gastric wall appeared thickened throughout the body. Microscopic examination revealed a colloid carcinoma in the region of the pylorus and lesser curvature. No tumor cells were found in the thickened wall of the body. The infiltration present there was inflammatory in character.

This case proved to be a type II carcinoma, and confirmed the gastroscopic diagnosis as to site and operability. Roentgen-ray examination indicated higher carcinomatous involvement, and the gross examination seemed to confirm this. However, microscopic examination showed this apparent involvement due to inflammation. As the surgeon stated, a more dangerous higher resection was therefore performed than if the gastroscopic limitation of the tumor had been accepted. This case bears out the statement made with respect to Case 1, that the gastroscopic appearance of a lesion is occasionally superior to the surgical and gross observation, and second only to the microscopic examination.

CASE 8. No. 118747 (described in detail elsewhere). A man aged 75 years had epigastric distress for 1 year, which was relieved by food. There was gastric anacidity and blood in the stools. Roentgen-ray examination revealed a penetrating ulcer of the lesser curvature with carcinomatous infiltration. The roentgenologist thought the extreme cardiac end of the stomach was not involved, but the examination was difficult because the patient could not relax. Gastroscopically, the tumor involved the lesser curvature, anterior wall, greater curvature, and the cardia. The patient expired five months later.

In this case, gastroscopy showed the definite inoperability of the carcinoma, and contemplated surgery was abandoned. In contrast, operability was correctly determined in the preceding Case 7 by the finding of a sharply limited tumor. Other such cases have been reported (37).

GASTROSCOPY AS A COMPLEMENTARY METHOD TO X-RAY

Gastroscopy cannot replace the x-ray in the study of gastric pathology. The two methods should not be considered competitive, but as complementary procedures (Jutras, Rigler, Schatzki, Templeton, 39). Roentgen-ray examination may be superior to gastroscopy in the diagnosis of an early, small carcinoma situated in the so-called "blind" gastroscopic areas. This is probably rare, since we have never seen such a case. However, we were not able to see a carcinoma, observed roentgenologically, which had produced an hour-glass formation. The gastroscope entered the upper "bag" only, and the tumor itself was not seen. In a case of previous gastric resection, prolapse of the jejunal mucosa into the stomach obscured a recurrent carcinoma, which was diagnosed roentgenologically. With very refined roentgen relief technique, using "spot" machines, the incorrect diagnosis of a very small carcinoma may occasionally be made, and gastroscopy may be able to rectify this error. The senior author has seen such cases in Munich.

The following two cases of large tumors show the two methods supplementing each other.

CASE 9. No. 190871. A man aged 42 years, seen January 4, 1938, had suffered gnawing epigastric distress for 6 months, 1 hour after meals. Diet and alkali afforded partial relief until December, 1937. Since then, weakness, loss of 4 pounds, vomiting, and loss of appetite had occurred. Physical examination was non-contributory. Hemoglobin was 78 per cent; red cell count, 4,500,000. Gastric content revealed lactic acid, and no free acid after an Ewald meal. After histamine, free acid (25) was present in 1 hour. Stools showed 4 plus occult blood.

Roentgen-ray and gastroscopic examinations were made January 17. A stenosing lesion of the pyloric end of the stomach and duodenal bulb was observed in roentgen-ray study. The impression was that of a probable peptic ulcer, although carcinoma could not be absolutely ruled out. However, the examination was unsatisfactory, and another was advised after aspiration.

On January 26, gastroscopy revealed a huge carcinomatous ulcer, type III, on the lesser curvature

along the angulus, with atrophic gastritis (Fig. 19, frontispiece). The tumor had a limiting, nodular wall toward the antrum and anterior wall, but the ulcer edge blended with the neighboring mucosa toward the lesser curvature, indicating infiltration. This infiltration extended upward to 2 to 3 centimeters below the cardia. The surrounding mucosa was atrophic. Operability was questioned, and the prognosis held poor even with a total resection.

Immediately following the gastroscopy, a second roentgen-ray examination was made. A diffuse carcinoma of the lesser curvature was diagnosed, within which a flat ulcer was present. The growth was thought to extend almost to the esophageal orifice.

Operation on January 31 revealed a large carcinoma on the lesser curvature, extending upward toward the cardia. The tumor was adherent to the transverse mesocolon and pancreas. A subtotal gastrectomy was performed, leaving a small stump of stomach behind, about 2 centimeters on the lesser curvature.

Pathological examination. Microscopically, a carcinoma simplex and extensive atrophic gastritis were observed.

The patient became rapidly weaker and expired May 11, 3½ months after operation.

The first roentgen-ray examination was unsatisfactory and failed to reveal the malignant character of the lesion, which was seen at subsequent gastroscopic examination. A second x-ray study confirmed the gastroscopic findings. The extent of involvement, the question of operability, and the ultimate prognosis were well answered by gastroscopy.

CASE 10. No. 203949.[1] A man aged 44 years, seen August 13, 1938, had suffered progressively increasing epigastric distress for 3 to 4 years. Beginning February, 1938, relief was obtained occasionally by induced vomiting. During the course of the illness, duodenal drainages were performed without improvement, a gall-bladder lesion being suspected. Roentgen-ray examinations in January, 1937, and in May, 1938, were negative. But on August 1, 1938, a defect was thought to be present on the greater curvature of the antrum, and a carcinoma was suspected. Gastric analysis showed the presence of free acid (20). Stools were occasionally positive for occult blood.

Gastroscopy (August 13, 1938). The pylorus was seen as a rigid dark hole. At the anterior wall of the antrum, separated from the pylorus by a small bridge of stiff mucosa, a large, round ulceration was seen. Its floor was a dirty gray. The edges were not entirely sharp. There was extensive infiltration along the lesser curvature and upper posterior wall. A definite demarcation was observed only on the anterior wall. Atrophic changes were seen at depth II (body). The diagnosis was that of a type III large carcinoma. Resection was considered technically possible, but the final prognosis held unfavorable.

Operation (August 20). On the lesser curvature of the stomach, extending up toward the cardia, an ulcerating carcinoma was present, approximately 2½ inches in diameter. Several involved lymph nodes were found along the lesser curvature. The liver appeared free of metastases. A high subtotal gastrectomy with entero-enterostomy was performed.

Pathological examination. Occupying the anterior stomach wall, and extending from the greater to the lesser curvature, was an ulcerated carcinoma, 5 by 2 centimeters, infiltrating the muscle wall and penetrating the serosa. Microscopically, there was an infiltrating, ulcerated adenocarcinoma, with involvement of lymph nodes. Atrophic gastritis, with metaplasia of epithelium, was prominent.

The symptoms present in this patient 3 to 4 years before examination seem to us to have been due probably to an atrophic gastritis. At the onset of induced vomiting, 6 months before gastroscopy, a carcinoma was very likely present. Roentgen-ray studies, made at a time when the tumor was certainly present (May, 1938), failed to reveal any disease. There is little doubt that the presence of a carcinomatous lesion would have been recognized gastroscopically without difficulty at that time, since the location of the lesion was one easily seen in gastroscopy, as was demonstrated in Cases 1 and 3, with gratifying results. Even shortly before gastroscopy, when an extensive lesion was present, the roentgen-ray findings were strongly suggestive, but not conclusive, of carcinoma. Gastroscopic examination settled any doubt as to the character of the lesion. Had gastroscopy been performed at the onset of symptoms, an atrophic gastritis might have been observed, periodic examinations advised, and the carcinoma perhaps discovered at an early stage.

SUMMARY AND CONCLUSIONS

1. Ten cases are presented to demonstrate the importance of gastroscopy in the diagnosis of gastric carcinoma. In 2, Cases 1 and 2, an early diagnosis was made, only gastroscopically, and in one of these the carcinoma was 8 by 2 millimeters in size. Two, Cases 3

[1] We are grateful to Dr. A. A. Goldsmith, Chicago, for referring the patient, and to Dr. A. A. Berg, New York City, for the operative report and pathological material.

and 10, showed the long developmental history, one of a small carcinoma (Case 3), the other of a large carcinoma (Case 10), the diagnosis being made conclusive by gastroscopy in both. In 3, Cases 4, 5 and 6, gastroscopy was important in the differential diagnosis between benign and malignant ulceration. Two, Cases 7 and 8, show the value of gastroscopy in the determination of operability. All show the need for co-operation between roentgenologist and gastroscopist.

2. The early diagnosis of gastric carcinoma may be possible if each patient over 35 years of age who suffers from mild digestive symptoms or loss of weight, otherwise unexplained, is examined roentgenologically and gastroscopically without delay. This is illustrated by Case 1.

3. The pathological concept, that gastric carcinoma in most cases develops on the soil of chronic gastritis, is corroborated clinically in Cases 1, 2, and 10, and especially in Case 3, in which no other sequence of events seems probable. Atrophic gastritis is evidently a precancerous condition and should be diagnosed. Except in such conditions as pernicious anemia, this can only be done gastroscopically.

4. Patients suffering from atrophic gastritis should be examined by roentgen-ray and by gastroscope at regular intervals, regardless of symptoms. A carcinoma producing symptoms is usually not of minimal size, particularly in the body of the stomach. The silent small carcinoma of Case 2, found in a patient with pernicious anemia and atrophic gastritis, would very likely have been discovered gastroscopically when it was one-half its actual size. In Case 3, a still earlier diagnosis might have been made if this rule had been followed. Therefore, *minimal-sized carcinomas may be found only by the routine periodic examination of patients with precancerous states.* Case 2, with repeated negative x-ray studies, demonstrates that gastroscopy may be an important additional procedure where the roentgen-ray results are negative or doubtful. Benign gastric tumor, which probably is related to atrophic gastritis, is also a precancerous condition, and such cases should be observed similarly. (See remarks following Case 3.)

5. An apparently benign gastric ulcer should be examined gastroscopically before medical treatment in patients over 35 years of age, since the malignant character of the ulcer may then be observed. During the course of treatment, the niche may become smaller during roentgen-ray observation, even though the lesion is malignant. The common belief that this decrease in size of the niche is evidence against malignancy, is wrong, as demonstrated in Cases 4, 5, and 6.

6. Gastroscopy has proved superior to roentgen-ray examination in determining the operability of certain cases. In Case 7, operability and favorable type were observed, in contrast to the roentgen-ray and even surgical findings. In Case 8, inoperability was definitely shown. Routine pre-operative gastroscopy may frequently eliminate exploratory operations for this purpose.

7. The gastroscopic picture has been found more characteristic than that of the gross specimen in 2 cases, owing to the presence of circulating blood. Only microscopic examination confirmed the important gastroscopic detail observed, in Case 1 as to the malignant nature of the lesion, in Case 7 as to the operability.

8. Gastroscopy and roentgen-ray examination are not competitive, but each supplements the other. Close co-operation between the gastroscopist and roentgenologist is essential, as existed in the presented cases.

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CYCLIC CHANGES IN CHROMATIN OF THE NUCLEI OF THE ENDOMETRIUM

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THE first observations on the lining of the uterus go back as far as Vesalius (48), although no real understanding of the structures and their significance was gained until about the middle of the nineteenth century. Modern investigation may be said to have begun with the work of Coste, 1847–1849, who demonstrated conclusively that the uterus is lined with a mucous membrane. The next significant advance was made by Kundrat and Engelmann who, in 1873, reported the results of a study of the histological changes associated with menstruation.

In 1896, Westphalen published an extensive article in which he correlated the days of the cycle and the structures in the endometrium, but the significance of his observations failed to impress his reading public, and perhaps even Westphalen himself. In 1908, Hitschmann and Adler published their paper which was to give new understanding and new impetus to the study of the female sex cycle. As a matter of fact, this paper contributed little additional data to the histology of the endometrium as previously recorded, but its significance lay in the fact that the authors recognized the cyclic nature of the structures they described. This realization and its emphasis made the paper of Hitschmann and Adler unique in gynecological investigation. The work of Schroeder (77, 78, 79) within the next few years further served to establish the truth of the concept of Hitschmann and Adler because he constantly referred to their work in his publications which were of wide clinical interest.

In the nineteenth century, contemporaneous with studies on the purely anatomical structure of the uterus, Dalton and later Leopold, published articles correlating the uterine and the ovarian structures, although their correlation was solely temporal and no causal concept was defined. In 1900, Knauer transplanted the ovaries of an animal and the results proved conclusively the endocrine nature of ovarian activity, while Fraenkel, Loeb, and Corner (24) proved experimentally that the corpus luteum of the ovary is essential for the uterine changes preceding and during the early part of pregnancy. This confirmation of the relationship of the corpus luteum to the uterus preceded by 20 years the establishment of the relationship of the follicle to the endometrium. In 1923, the hormone produced by the follicle was prepared from the follicular fluid and its effect upon the genital tissues was observed. This work, initiated by Allen and Doisy in the United States and by Butenandt in Germany, has resulted in a tremendous amount of research in the clinic and laboratory which has proved indubitably that the follicular hormone is responsible for growth of the genital tissues in general (1), and especially of the endometrium (1, 20, 31, 39, 54, 55, 98, 108).

The ovarian-uterine interrelationship once firmly established has meant, in practical application, that the microscopic structure of the endometrium yields accurate information concerning the hormonal activity of the ovary. This is possible because of the specificity of the follicular hormone in producing growth, and of the corpus luteum factor in producing secretion (4, 20, 25) in the cells of the endometrium.

The ovary, for lack of definite proof to the contrary, was generally believed to be more or less autonomous until that epoch-marking year of 1926 when Smith (87, 88) in the United States, and Zondek and Aschheim (106, 107) in Germany, demonstrated that the ovary is stimulated by substances secreted by the pituitary gland. Even greater volumes of work appeared on the pituitary-ovary relationship on the basis of this work than have

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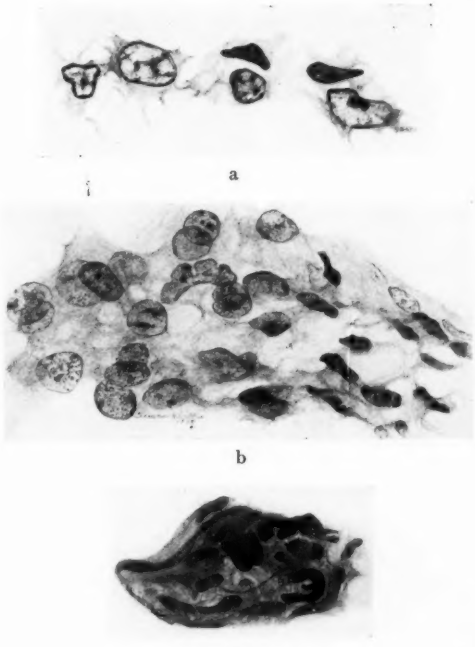

Fig. 1. Stromal cells. a, Granular and non-granular form of nucleus represented. The granular nuclei have smooth and irregular contours. b, Stromal cells from the transitional zone between basalis and spongiosa. Note the solid chromatin in the nuclei on the right which is in the region of the basalis, and the granular chromatin in the nuclei on the left. The canals between the cells have been described by Young. c, Typical basalis region containing the solid homogeneous non-granular chromatin in the nuclei of irregular contour.

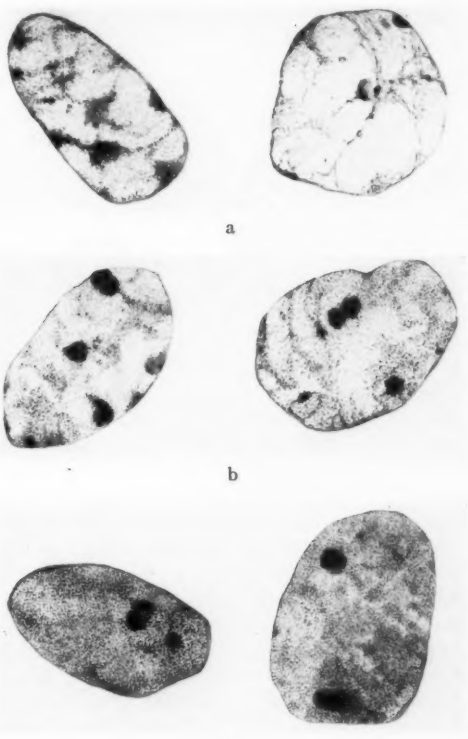

Fig. 2. Granular nuclei. a, Aggregated chromatin. This type of nucleus predominates in specimens of proliferative endometrium. The chromatin particles are aggregated along lines approximating those described for the linin network. The unstained nucleoplasm between the aggregated chromatin strands contains but few of the discrete chromatin particles. b, There are many discrete particles of chromatin scattered through the unstained nucleoplasm in this type of nucleus which is intermediate between the typical aggregate and the typical diffuse type of granule distribution. c, The chromatin particles are distributed diffusely throughout the unstained nucleoplasm. There may be two or more large round or oval areas of solid chromatin present in nuclei of this type. There is little or no hint of the outline of the linin network.

appeared on the ovarian-uterine relationship. As a result of these extensive investigations it has been definitely shown that two specific pituitary factors act upon the ovary (21, 36, 104, 106). The first, and apparently the more fundamental and abundant, is a substance stimulating the growth of ovarian follicles (95, 104); the second, a factor which brings about transformation of the granulosa and thecal cells in the ovary into corpus luteum cells (36, 95, 104, 105). As though this relationship is not sufficiently complicated, it has been further shown that the follicular hormone produced in the ovary as a result of pituitary stimulus, in turn acts back on the pituitary (6, 33, 59, 60, 68, 69, 81) and affects the amount of follicle stimulating factor released, as well as the amount of the luteinizing factor (30, 35, 51, 100, 101). At least to date no adequate evidence of a uterine hormone has been brought forth to complicate further the interrelationships in solving the *modus operandi* of the sex cycle.

The anatomist and the endocrinologist have demonstrated that the normal function

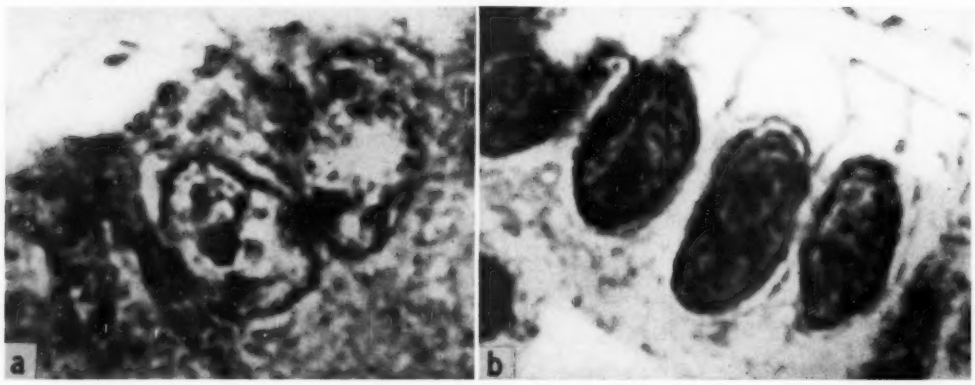

Fig. 3. a, Specimen No. 4929. Showing gland epithelial nuclei which contain aggregate chromatin. 2 mu section. Bouin fixation. Wratten plate. ×3000. b, Specimen No. 4640. Showing gland epithelial nuclei which contain diffuse chromatin. 2 mu section. Bouin fixation. Wratten plate. ×3000.

of the sex cycle depends upon the proper balance between ovary and pituitary. But the clinician has contributed no small part of the present knowledge of the uterine cycle. Schroeder (78, 79) in 1912 reiterated a previously enunciated concept (11, 18, 28, 43, 76) that pathological endometrial pictures accompanying menstrual dysfunction are the result of ovarian disorders. Confirmation of the rôle of the ovary in producing the classical picture of glandular cystic hyperplasia (39) came in 1931 and 1932 when Burch and his coworkers (15, 16, 102) produced the condition experimentally. This work, subsequently repeated by others (55, 75, 92, 98, 108), has formed a basis for the analysis and therapy of ovarian disorders as manifested by endometrial pathology and menstrual symptoms (13, 14, 19, 20, 54, 55, 96), as well as forming a basis for the experimental reproduction of the various pathological pictures (75, 83, 84, 92).

Repeated studies and investigations of endometrial structure have established certain histological characteristics as criteria in determining the secretory, proliferative, or menstrual nature of endometrium. Hitschmann and Adler based their differentiations of the endometrium in the different phases of the cycle largely on gland form and the progressive thickening of the mucosa; Schroeder (77) described cellular and internal cytoplasmic pressure variations during the cycle. Hitschmann and Adler classified endometrial tissues as characteristic of a postmenstrual phase, an interval phase, a premenstrual phase, and a menstrual phase. Schroeder's classification (79) of endometrial tissue was based on the histophysiological characteristics of regeneration and proliferation (corresponding to the temporal phase of postmenstrual and interval), secretion (the premenstrual phase), and desquamation (menstruation). The basic characteristics of endometrial structure in the different phases of the menstrual cycle, together with the menstrual history, have made possible a knowledge of the successive stages of the development of the endometrium from one menstrual phase to the next. The essential criteria for these stages have been included in the following review of the literature on the histology of the endometrium.

Histology of the endometrium. The lining of the uterus is unique, not only because of its periodic desquamation, but also because of the rapidity of its growth and its modification from an essentially proliferative tissue to one that is essentially secretory in nature.

These uterine tissues so responsive to hormonal stimuli consist of an extremely sensitive gland and surface epithelium, and a less reactive, connective tissue stroma (77, 80) through which blood vessels and lymphatics course. The form of the glands, and of the

cells comprising them, present typical histological pictures characteristic of growth and of secretion. The two outer reactive regions of endometrial tissue are known as the functional layers and the region next the uterine muscle, which is not affected by the cyclic variations of the hormones, is known as the basalis.

Proliferative endometrium (postmenstrual and interval). The endometrium in the period immediately following desquamation and in the interval preceding ovulation is essentially a growing endometrium. The literature contains many references to and descriptions of postmenstrual, early, mid and late interval types of tissue, with careful observations on the differences between them, but the basic characteristic common to all of these tissues is that of cellular increase by mitotic division. The gland and connective tissue modifications described for the early, mid, and late interval types of endometrium are merely the result of this cell proliferation in varying degrees. The endometrium progressively thickens throughout the period preceding ovulation (50), and there may be a differentiation into the superficial compacta and deeper spongiosa layers (50). The stromal connective tissue is composed of an acellular fibrillar network in the meshes of which lie stellate or spindle shaped connective tissue cells (34, 50, 52, 56, 78, 103). When there is a differentiation into the compacta and spongiosa, the connective tissue cells are more numerous in the compacta, more sparse in the spongiosa (82), while the fibrillar network is more dense in the compacta, and looser meshed in the spongiosa. The lumen of the glands in the compacta is relatively narrow in both the proliferative and secretory phases of the cycle (50). These narrow lumened glands, initially straight from fundus to mouth throughout the depth of the endometrium (50, 74, 99), become somewhat twisted and slightly tortuous in form as the proliferative phase progresses (50, 99). This is true especially in the region of the spongiosa with its paucity of connective tissue cells and wide meshed fibrillar network (80). Mitotic figures are reported in the stroma of postmenstrual and proliferative tissue (50, 56, 70, 99). The glands are relatively few in number in the period immediately following desquamation (50, 70, 78), and their progressive increase in number is attributed to the growth of buds of epithelial cells from strands of epithelium connecting the fundic portions of the existing glands in the basalis (74). This mode of gland increase by epithelial growth apparently is not limited to the proliferative phase of the cycle since there is histological evidence that the basal buds continue to extend themselves toward the uterine lumen during the secretory phase of the cycle (74a, 74b).

The epithelial cells increase so rapidly as a result of the extensive mitosis that the cells are piled upon one another and are pseudostratified (50, 70, 77, 78, 99). The amount of cytoplasm in these cells is slight (70), and there is little histological evidence for secretory activity (50, 70, 80). The cytoplasm is acidophilic (80), with a sharply defined cell membrane (50, 77). Areas of modified cytoplasm or vacuoles may be seen in some cells either beneath or beside the nucleus (50, 77, 78). When secretory products are present in the lumen of glands during the proliferative phase of the cycle, they lie immediately next to the lumen edge of the cell membrane which is sharply defined (50, 70, 77, 78); this appearance is so characteristic for the phase, that such cells are described as type I secretory cells (8). Type I secretory cells may also be seen in tissues secured during the secretory phase of the cycle, but they occur in greater numbers during the proliferative phase (8, 78). The nuclei of the epithelial cells are large and elliptical (50, 70) with sharply staining chromatin (50, 70); they may be basally or centrally located within the cell (50, 77, 82). Large numbers of mitotic figures are present in the epithelium during this phase of the cycle (50, 70, 77, 99).

The scope and purpose of this paper does not appear to justify a discussion of the reports in the literature of the Golgi apparatus (9, 19, 94), ciliated cells (8, 34, 44, 80), glycogen (9, 10, 74, 74b, 80, 91, 97),[1] lipoid content (5, 45, 99), and mitochondria (8, 9) since

[1] Since the writing of this, a paper by Hisaw and Greep has appeared in Endocrinology, 1938, 23: 1–14 which contains descriptions of the glycogen content of the endometrium of castrate monkeys following treatment with estrin and progestin.

they must be studied by use of special techniques.

Secretory or premenstrual endometrium. The most striking differences in the appearance of a typical proliferative endometrium and of a typical secretory endometrium lie in the form of the glands (50) and in the cells comprising them (77), as well as in the relative thickness of the tissue (50). The glands are widely dilated with an irregular serrated outline and are often described as dentate (50, 74, 99). The entire tissue is edematous (50, 99), especially in the spongiosa where the stromal cells are sparse, and spindle-shaped (50, 82). The compacta region, as the name implies, is relatively dense and the distal portion of the glands passing through this region retain the straight narrow form characteristic of the proliferative period (50, 82). The stromal cells of the compacta are enlarged round structures with a definite rim of cytoplasm (50, 70, 80). Their resemblance to the form of the stromal cells in the compacta region during early pregnancy was long ago recognized, and the term "decidual" was employed in describing them (50). Mitotic figures may be seen in the stroma of some specimens (74).

The cells comprising the epithelium of the glands are usually of the simple columnar type (50), although in specimens of typical secretory endometrium there may be areas of the gland walls and even entire glands which are composed of pseudo-stratified cells characteristic of the proliferative type of epithelium (50, 78). The dilated lumen of the glands of a secretory endometrium contain products of secretion and cell débris (50, 99). The cell membrane is often indistinct and stains poorly (78). The cytoplasm of the cell may be so great that the free surface of the cell projects into the gland lumen in a typical club-shaped form (77). Where a group of epithelial cells of this form occur the histological picture produced is described as tufting (50, 70, 78), and it is one of the outstanding characteristics of a true secretory endometrium. The club-shaped, distended cell of the secretory endometrium is so typical for this phase of the cycle that it has been referred to as a type II secretory cell in contrast to the type I cell seen chiefly in the proliferative tissue (8). The nuclei are large (74a), round (77), pale-staining (9) structures, well separated from one another (50), and they may be basally or centrally located within the cell (50).

Menstrual endometrium. Immediately preceding and during menstruation there are great numbers of leucocytes infiltrated throughout the stromal cells and penetrating between the cells of the gland epithelium (50). Great numbers of pycnotic or solid chromatin nuclei may be seen among the stromal cells (8, 50). The glands of a late secretory menstrual endometrium are often collapsed (50) and the epithelial cells are low columnar or cuboidal in form with a frayed cell membrane on the lumen edge of the cell (50, 77). The cytoplasm of these cells is pale staining (50, 82); the nuclei are pale blue in color (50) when stained with hematoxylin. No mitotic figures in menstrual stroma (50).

Anovulatory menstrual endometrium. Investigation has shown that in some instances normal bleeding may occur from an endometrium which gives no histological evidence of the presence of a corpus luteum hormone. The concept of normal anovulatory bleeding (i.e., bleeding following a 28 day interval during which follicle rupture failed to take place, and as a consequence normal corpus luteum formation also failed) is supported by experimental (1, 22, 23, 25, 47, 49) and clinical evidence (3, 8, 90). This finding explains the small percentage of instances in the descriptions of menstrual specimens in which the tissue characteristics are definitely of a proliferative nature, with no secretory manifestations, while the protocols indicate a previous cycle of normal length (50, 56, 61, 99).

Transitional types of endometrium. Tissues containing some characteristics of both a secretory and a proliferative endometrium are frequently encountered and an accurate diagnosis of the types of ovarian hormones acting on the endometrium is possible when the characteristics of the tissue are correlated with the time in the cycle at which the specimen was secured. Thus the terms "early secretory," "late secretory," and "post-menstrual-early interval" have come into use.

Pathological endometrium. Among the numerous descriptions in the literature of speci-

mens of pathological endometrium secured from patients manifesting marked changes in the nature of the menstrual cycle, Schroeder's (78, 79), in 1912 and subsequently, stand out today because he emphasized a concept, previously enunciated (11, 18, 28, 43, 76), that disorders of ovarian function produce the pathological pictures seen in the endometrium. His descriptions of tissues secured from patients presenting progressively marked menstrual disorders clearly show that he considered glandular cystic hyperplasia the result of extreme proliferative activity and that the less severe menstrual disorders and the accompanying endometrial pictures were intermediate between normal conditions and the bleeding hyperplasia. In the order of increasing pathology he described tissues showing, (1) slight, but not a normal degree of secretory modification; (2) others which showed no secretory activity whatever; (3) others with an excessive degree of pseudostratification of the gland epithelium but without unusual twisting or dilatation of the glands; and (4) the frank glandular cystic hyperplasias. Schroeder's work, and that of others, has shown both clinically and experimentally that excessive proliferation of endometrial tissue is the result of the loss of the secretory phase of the cycle (7, 15, 16, 55, 75, 92, 98, 102, 108).

PRESENT INVESTIGATIONS

Recent investigations have shown that the endometrium undergoes progressive changes as a result of modifications in ovarian secretion (13, 38, 65, 67, 71, 72, 73, 89, 93). These may be classified as (1) a dimunition in the amount of corpus luteum secretion, (2) an absence of corpus luteum secretion, and (3) an absence of both corpus luteum and follicular hormone secretion (12, 13). Since these histological changes in the endometrium are a quantitative reflection of the endocrine activity as a whole, it is important to differentiate between the types of endometrium resulting from the various types of ovarian failure. This is possible in many instances, but in a certain percentage of the cases it is impossible to diagnose the specimens satisfactorily. In general, the greatest difficulty is encountered in that group of tissues which deviates only slightly from the normal, and also in the group of tissues in which it is impossible to state if there is any corpus luteum effect manifested in the tissue at all. This investigation was undertaken in the hope of recognizing histological characteristics which might furnish additional criteria for differentiating between a normal and a very mild first degree failure, and between a severe first degree and a mild second degree failure endometrium.

Since the endometrium grows rapidly, secretes, and desquamates, it seemed probable that cellular rather than tissue characteristics might yield some clue which would aid in determining the nature of the tissue changes. Previous work has clearly shown that mitotic activity is high in the endometrium during the growth of the follicle in the ovarian cycle, lower during the corpus luteum phase, and absent entirely at the time of menstruation. It was, therefore, not surprising to find that specific differences in chromatin form and distribution could be demonstrated within the nuclei of the endometrium secured during the various phases of the menstrual cycle.

Material and methods. Two hundred specimens of endometrium which had been secured through operative procedure and by the punch biopsy technique, were chosen at random from the files of the department of obstetrics and gynecology. As a routine procedure, all tissues in this laboratory are promptly fixed in Bouin's fluid and stained with hematoxylin. The entire study was made with the aid of oil immersion lens (N.A.1.30) and 12.5× and 25×oculars. The studies of the stroma were entirely completed before the epithelium was examined. A crude method of determining the proportions of various types of nuclei in the stroma of the functional layers in the specimens was developed by placing a glass disc with a centimeter square etched on it into the 12.5×ocular and counting a minimum of 300 cells per specimen. Fields were chosen indiscriminately from the functional layers of the stroma; areas of trauma, hemorrhage, and compression were avoided as much as possible.

These tissues had been routinely classified by the department of obstetrics and gynecology as (1) normal endometrium showing

TABLE A.—CLASSIFICATION BY THE DEPARTMENT OF OBSTETRICS AND GYNECOLOGY OF THE TISSUES EMPLOYED IN THIS STUDY

	No. of specimens
Histologically normal endometrium	
Proliferative phase	7
Secretory phase	14
Menstrual, day 1 and 2, phase	4
Pathological endometrium	
Weak progestin—first degree failure—	
Proliferative phase	0
Secretory phase	10
Menstrual, day 1 and 2, phase—short cycle, 15; long cycle, 5; normal cycle, 26	46
No progestin—second degree failure—	
Hyperplasia	17
Secretory phase	0
Menstrual, day 1 and 2, phase	0

either secretory, proliferative, or menstrual characteristics (four were designated as postmenstrual); (2) pathological endometrium showing some, but not a full, effect of the corpus luteum hormone, and designated as first degree failure (either menstrual or secretory); and (3) pathological endometrium manifesting an exaggeration of the action of the follicular hormone, with no corpus luteum action on the tissue being apparent histologically; these latter tissues were hyperplastic in nature and classified as second degree failure.

A preliminary correlation of the chromatin form in the glands of all secretory specimens, whether normal or pathological, and of all proliferative tissues, whether normal or pathological, was made to determine if there was adequate evidence that one type of chromatin appeared consistently in either type of tissue. A second preliminary correlation of the chromatin in day 1 menstrual specimens, regardless of normal or pathological structure but grouped according to the length of the preceding cycle, was made to determine if cycle length might be a factor upon which structure of menstrual tissues depended. Following this, the normal tissues were subdivided into the proliferative, secretory, and menstrual groups and analyzed for chromatin form in glands and stroma. These factors were then compared with the same ones in the first degree failure menstrual and first degree failure secretory tissues, as well as in the hyperplastic specimens, and in a special group of bleeding specimens. Because of the large number of first degree failure menstrual specimens, the menstrual history was consulted and the specimens divided into those which were secured after short cycles, after cycles of normal length, and after lengthened cycles (Table A.)

Findings. There were two distinct forms of chromatin in the nuclei of the endometrium. It occurred as finely divided particles in a clear nucleoplasm, or as a solid homogeneous mass of chromatic material which was irregular in outline and was similar in appearance to that of the nuclei in the basalis region (Fig. 1, a, b, and c). These solid homogeneous nuclei have been described in the literature as "pycnotic" (56), and as occurring in greatest abundance in specimens of menstruating endometrium (50, 56).

The granular chromatin (64) was distributed either diffusely or irregularly throughout the clear nucleoplasm. In the diffuse type of distribution, the particles of chromatin were lying equidistant from one another within the nucleoplasm which also contained one or more large round or oval masses of solid homogeneous chromatic material. Nuclei of this type appeared to be pale blue in color, and have been described in the literature as having "fine" (32, 37), or "diffuse" (53) chromatin (Fig. 2, c; Fig. 3, b).

When the granular chromatin was irregularly distributed within the clear nucleoplasm, large numbers of these granules were aggregated along lines approximating those described for the linin network.[1] At intervals along this network there were large polygonal areas of discrete chromatin particles. Between the strands of aggregated chromatin there were a few granules lying free in the colorless nucleoplasm. The relationship of the granules of chromatin to the lines approximating those for the linin network resembled that of iron filings to the lines of force created by a magnet. In the literature (37), the term coarse chromatin has been applied to nuclei of this type (Fig. 2, a; Fig. 3, a).

The frequency of mitotic figures was greatest in groups of tissues in which the granular chromatin was aggregated and least in those in which the chromatin was diffusely distributed (Table I, Charts 2, 3, 7, and 8).

[1] Heape (1894) reported that a network is always seen in the nuclei of the endometrium in the "resting" stage (the interval or proliferative stage of later investigators). He states that at other times the network is less pronounced and frequently invisible, at which times the nuclei are pale staining and have a dark staining nucleolus at the base of the nucleus.

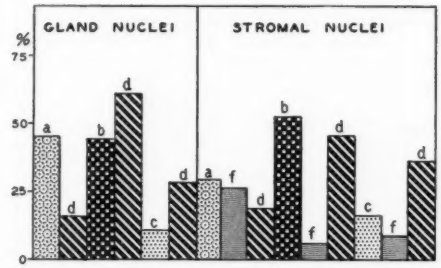

Chart 1. Association of types of granule distribution in nuclei with the presence of solid chromatin nuclei and with the presence of mitotic figures. a, Percentage of 185 specimens having diffuse; b, percentage having aggregate; c, percentage having intermediate type of chromatin; f, percentage average of solid nuclei in stroma of tissues containing the various types of granule distribution, based on cell counts; d, percentage of specimens in each group having mitotic figures.

In many specimens the granular chromatin was of neither the typically diffuse type of distribution nor of the typically aggregate, but was apparently a variation of one or the other of these two. An analysis of the difference in appearance between these intergrades and the typical diffuse or typical aggregate, revealed that the relative abundance of the discrete particles of chromatin in the colorless nucleoplasm was responsible for the varying appearances (Fig. 2, b).

Gland nuclei. The gland nuclei rarely contained the solid homogeneous form of chromatin; when present, it was in cells which have been described in the literature as "rod" cells. The granular nuclei almost uniformly had smooth even contours, although in some specimens they were somewhat crumpled and irregular in outline.

Stromal nuclei. The stromal nuclei presented a much more varied picture than the epithelial nuclei. Frequently, this could be traced to the presence of large numbers of nuclei with the solid homogeneous type of chromatin; and again, the difference depended upon the relative proportions of nuclei with smooth, and nuclei with crumpled, nuclear membranes. The varying proportions of granular to solid chromatin nuclei, and of smooth contour to irregular contour granular nuclei, furnished a basis for tissue differentiation independent of gland form or menstrual history. The solid chromatin nuclei occurred more frequently in tissues containing the diffuse granular chromatin than in those containing the aggregate granules of chromatin (Table I, Chart 1).

TABLE I.—ASSOCIATION OF MITOSIS AND GRANULAR CHROMATIN DISTRIBUTION IN GLAND EPITHELIUM AND OF SOLID HOMOGENEOUS NUCLEI WITH THE VARIOUS TYPES OF CHROMATIN DISTRIBUTION IN THE STROMAL NUCLEI IN 185 TISSUES

Area of tissue	Type of chromatin distribution		
	Diffuse	Intermediate	Aggregate
Gland epithelium No. of specimens	83	21	81
Per cent mitosis	15.6	28.7	61.7
Stroma No. of specimens	56	30	99
Per cent mitosis	19.6	36.7	45.5
Per cent average of solid nuclei in cells counted	27	9.5	6.6

Generally one type of granular chromatin distribution prevailed throughout a single specimen, i.e., in both glands and stroma it was either all of the diffuse or all of the aggregate type of distribution, or all of some uniform intergrade between these extremes. In some tissues there were differences in the type of granule distribution in the compacta and spongiosa layers of tissue.

Too much emphasis cannot be placed upon the fact that these studies on nuclear form were made with the aid of the oil immersion lens, and that the tissues were not previously examined under low or even high dry objectives by the investigator in order that histological criteria of proliferation and secretion should not in any way influence the necessarily subjective decision as to the character of the nuclei. At the completion of the study, the chromatin form in the gland nuclei, and the occurrence of mitotic figures, were correlated with the nature of the tissue reaction as recorded in the files of the department of obstetrics and gynecology.

PRELIMINARY CORRELATION OF GRANULAR CHROMATIN WITH SECRETORY AND PROLIFERATIVE TISSUES

Gland chromatin in all postmenstrual and proliferative tissues. These tissues were char-

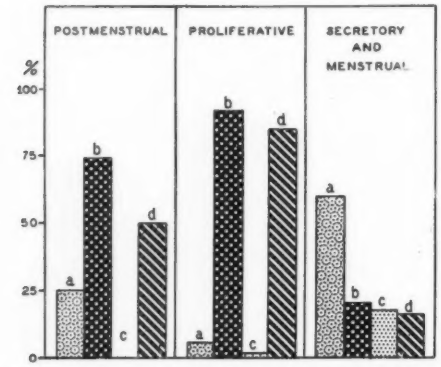

Chart 2. Chromatin granule distribution and mitosis in gland nuclei of specimens of endometrium as classified by the Department of Obstetrics and Gynecology. a, Percentage of specimens having diffuse chromatin in gland nuclei; b, percentage of specimens having aggregate chromatin in gland nuclei; c, percentage of specimens having intermediate type of granule distribution in gland nuclei; d, percentage of specimens in group having mitotic figures in gland nuclei.

acterized by the presence of the aggregate type of granule distribution in the gland nuclei and also by the large number of specimens which had mitotic figures in the gland nuclei (Table II, Chart 2).

Gland chromatin in all secretory and menstrual tissues. Since there were no outstanding differences in the figures compiled on all the specimens pronounced as having secretory characteristics and all those simply listed as menstrual in character, the data on these two groups of tissue have been combined and presented in one column. There was a great increase in the number of specimens containing the diffuse type of granular chromatin in the

TABLE II.—CLASSIFICATION OF SPECIMENS ACCORDING TO DEPARTMENTAL RECORDS

Diagnosis	No. of specimens	Granule distribution in gland nuclei			No. having mitosis in glands
		Diffuse	Aggregate	Intermediate	
Postmenstrual	4	1*	3	0	2
Proliferative	52	3†	48	1	45
Secretory and menstrual	129	77	28	24	21
Unclassified	15				

*Day 10 after 28 day cycle in a 33 day cycle.
†2 of these secured on day 8 after onset of previous bleeding, 1 secured on day 15.

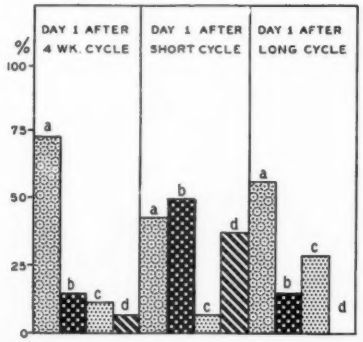

Chart 3. Chromatin granule distribution and mitosis in gland nuclei of day 1 menstrual specimens secured after cycles of different length. a, Percentage of specimens having diffuse chromatin, and b, percentage of specimens having aggregate chromatin in gland nuclei. c, Percentage of specimens having intermediate type of granule distribution in gland nuclei. d, Percentage of specimens having mitotic figures in gland nuclei.

gland nuclei in these specimens as compared with those of the proliferative group, and there was a marked decrease in the number of specimens containing the aggregate type of granular chromatin. The number of specimens containing mitotic figures in the gland nuclei was much less in the secretory tissues than in the proliferative tissues (Table II, Chart 2).

Gland chromatin in all day 1 menstrual specimens. The day 1 menstrual specimens, regardless of the length of the preceding cycle, were characterized by the presence of diffuse chromatin in the gland nuclei in the majority of cases. When the tissues were grouped according to the length of the preceding cycle, the day 1 tissues secured after short cycles of 1

TABLE III.—CHROMATIN FORM IN GLAND EPITHELIUM OF 49 DAY 1 MENSTRUAL SPECIMENS AFTER CYCLES OF NORMAL, SHORT AND PROLONGED LENGTH

Length of cycle	No. of specimens	Granule distribution in gland nuclei			No. having mitosis in glands
		Diffuse	Aggregate	Intermediate	
Normal length	26	19	4	3	2
Short cycle	16	7	8	1	6
Long cycle	7	4	1	2	0
Total	49	30	13	6	8

and 2 weeks tended to have the aggregate chromatin more often than the diffuse type, and mitotic figures were present in more tissues of this group than in the ones secured after cycles of average or of prolonged length (Table III, Chart 3).

HISTOLOGICALLY NORMAL ENDOMETRIUM

Twenty-five specimens included in this study which were described as having a normal histological structure were secured during a cycle which subsequently proved to be of normal length, and the cycle preceding had been of normal length. The specimens were obtained on the various days of the cycle dating from the onset of the previous bleeding, but the number and distribution of these specimens over the days of the cycle is such that no great significance with reference to cyclic variations can be attached to the observations reported (Table VIII).

Proliferative tissues. Gland nuclei. Aggregate chromatin and mitotic figures characterized the gland epithelium of these tissues (Table VIII, Chart 7). Two exceptions occurred in specimens secured on days 8 and 10, respectively, the former was described as an interval specimen, the latter as a postmenstrual one. There are several reports in the literature in which "atypical" specimens of endometrium are described (56, 74a, 77), and in some of these reports, the atypical specimens have been discarded in the general review of the findings by these investigators. Although the number of such reports is not great, the dating of the specimens is usually unquestioned, and they should not be dismissed too lightly. *Stromal nuclei.* The granular nuclei in the stroma likewise was of the aggregate type in the majority of instances (Table VIII, Chart 8). There were fewer specimens having mitotic figures in the stroma in the proliferative than in the secretory specimens (Chart 8). There were more nuclei having smooth contours in the stroma of the group of proliferative than in the group of menstrual tissues, but there were fewer nuclei with smooth contours in the proliferative than in the secretory tissues (Table VII, Chart 9). There were few or no solid "pycnotic" nuclei in the stroma of the proliferative specimens, with exception of tissues that did not have the aggregate form of granular chromatin; in these, the numbers of "pycnotic" nuclei were higher (Table VIII).

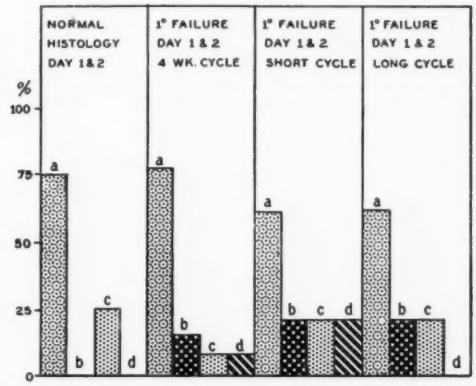

Chart 4. Chromatin granule distribution and mitosis in gland nuclei of normal day 1 and 2 menstrual specimens, and of first degree failure day 1 and 2 menstrual specimens as diagnosed by the Department of Obstetrics and Gynecology. a, Percentage of specimens having diffuse and b, percentage of specimens having aggregate chromatin in gland nuclei. c, Percentage of specimens having intermediate type of granule distribution in gland nuclei. d, Percentage of specimens having mitotic figures in gland nuclei.

TABLE IV.—FREQUENCY OF OCCURRENCE OF DIFFERENT TYPES OF CHROMATIN IN GLAND NUCLEI OF DAY 1 AND 2 MENSTRUAL SPECIMENS OF NORMAL AND FIRST DEGREE OVARIAN FAILURE PATIENTS

Tissue diagnosis	Length of previous cycle	Days	No. of specimens	Chromatin distribution in gland nuclei—per cent			Specimens having mitosis—per cent
				Diffuse	Aggregate	Intermediate	
Normal	av. 4 wks.	1 & 2	4	75	0.0	25.0	0.0
1° failure	av. 4 wks.	1 & 2	26	77	15.3	7.7	7.6
1° failure	3 wks. & less	1 & 2	15	60	20.0	20.0	20.0
1° failure	5 wks. & more	1 & 2	5	60	20.0	20.0	0.0

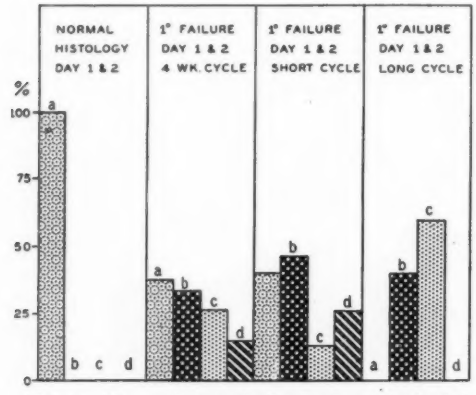

Chart 5. Chromatin granule distribution and mitosis in stroma nuclei of normal day 1 and 2 menstrual specimens, and of first degree failure day 1 and 2 menstrual specimens secured after cycles of different length. a, Percentage of specimens having diffuse and b, percentage of specimens having aggregate chromatin in stroma nuclei. c, Percentage of specimens having intermediate type of granule distribution in stroma nuclei. d, Percentage of specimens having mitotic figures in stroma nuclei.

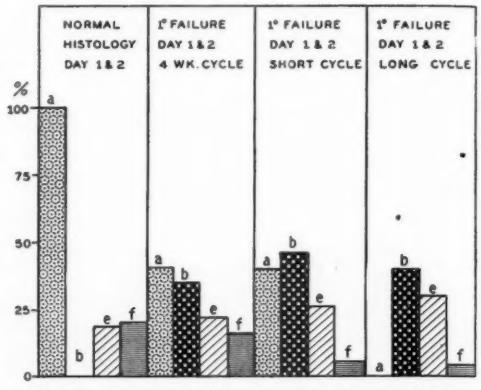

Chart 6. Stroma studies: chromatin granule distribution and per cent average of solid nuclei and of granular nuclei with smooth contour in normal day 1 and 2 and in first degree failure day 1 and 2 menstrual specimens secured after cycles of different length. a, Percentage of specimens having diffuse, and b, percentage of specimens having aggregate chromatin in stroma nuclei. e, Per cent average of granular nuclei with smooth contours in the stroma of the specimens in the group, based on cell counts. f, Per cent average of solid chromatin nuclei in the stroma of the specimens in the group, based on cell counts.

Secretory tissues. Gland nuclei. In the secretory specimens, the gland nuclei contained the intermediate and diffuse type of chromatin in the majority of the specimens (Table VIII, Chart 7), and mitotic figures appeared in many of them. *Stromal nuclei.* In the normal secretory tissues there were fewer specimens with the diffuse type of chromatin in the stroma than in the gland epithelium. More specimens of this group contained mitotic figures in the stroma than in the gland epithelium (Table VIII, Chart 8). There were more smooth contour nuclei in the stroma of the secretory tissues than in the stroma of the proliferative or menstrual tissues of the normal groups (Table VIII, Chart 9). Tissues secured on sixteenth and twenty-third days after onset of previous menstruation contained large numbers of solid homogeneous nuclei in the stroma (Table VIII).

Menstrual, day 1 and 2. There was no aggregate chromatin in either the gland or stromal nuclei, and no mitotic figures in any of the tissues included in this classification. The nuclei with smooth contours were fewer in number in the stroma of the menstrual tissues than in either the proliferative or secretory tissues, while the numbers of solid "pycnotic" nuclei were greater than in any of the other tissues of the normal group (Table VII, Chart 9).

TABLE V.—STROMAL NUCLEI IN DAY 1 AND 2 MENSTRUAL SPECIMENS FROM NORMAL AND 1° OVARIAN FAILURE PATIENTS

Tissue diagnosis	Length previous cycle	Days	No. of specimens	Chromatin distribution in stromal nuclei—per cent			Nuclear form in stroma		Specimens having mitosis—per cent
				Diffuse	Aggregate	Intermediate	Av. % smooth nuclei	Av. % solid nuclei	
Normal	4 wks.	1 & 2	4	100.0	0.0	0.0	19.0	20.4	0.0
1° failure	4 wks.	1 & 2	26	38.4	34.7	26.9	22.8	16.5	15.0
1° failure	short	1 & 2	15	40.0	46.7	13.3	26.3	5.7	26.0
1° failure	long	1 & 2	5	0.0	40.0	60.0	30.4	4.2	0.0

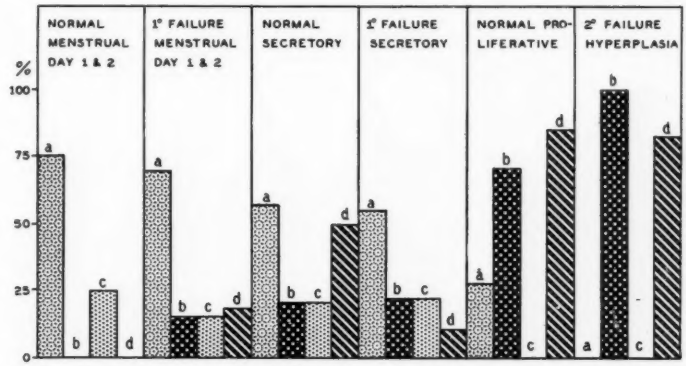

Chart 7. Chromatin granule distribution and mitosis in gland nuclei of normal and abnormal types of endometrium. a, Percentage of specimens having diffuse and b, percentage of specimens having aggregate chromatin in gland nuclei. c, Percentage of specimens having intermediate type of granule distribution in gland nuclei. d, Percentage of specimens in group having mitotic figures in gland nuclei.

COMPARISON OF CHROMATIN FINDINGS IN NORMAL AND PATHOLOGICAL ENDOMETRIUM

When the nuclear form and structure in pathological tissues was compared with that of tissues having normal histological structure, the pathological tissues were classified as those showing some secretory characteristics (first degree failure) and those showing no secretory activity (second degree failure). The first degree failure tissues were grouped into day 1 and 2 menstrual for comparison with the normal day 1 and 2 menstrual, and the remaining first degree failure tissues compared with the normal secretory specimens. The second degree failure tissues were grouped for comparison with normal proliferative specimens.

Normal menstrual and first degree failure menstrual tissues. When the 4 normal specimens of menstrual endometrium were compared with the 46 first degree failure menstrual tissues, no especially marked differences between the gland nuclei of the two groups could be distinguished, with the exception that there were some of the first degree tissues which had mitotic figures in the gland epithelial nuclei, and a few such specimens with the aggregate type of granular chromatin (Table VI, Chart 7). When the 46 first degree failure day 1 and 2 tissues were subdivided according to the length of the preceding cycle, there was even less contrast between the gland nuclei of the normal and of the first degree failure specimens secured after cycles of approximately 4 weeks (Table IV, Chart 4). There were mitotic figures in the gland epithelium of some of the first degree failure menstrual specimens secured after

TABLE VI.—GLAND CHROMATIN DISTRIBUTION IN NORMAL AND PATHOLOGICAL SPECIMENS OF ENDOMETRIUM

Tissue diagnosis	Tissue reaction	No. of specimens	Chromatin distribution in gland nuclei—per cent			Specimens having mitosis—per cent
			Diffuse	Aggregate	Intermediate	
Normal	Menstrual	4	75.0	0.0	25.0	0.0
1° failure	Menstrual	46	69.6	15.2	15.2	18.0
Normal	Secretory	14	57.1	21.4	21.4	50.0
1° failure	Secretory	9	55.0	22.5	22.5	11.0
Normal	Proliferative	7	28.6	71.4	0.0	85.0
2° failure	Proliferative	24	0.0	100.0	0.0	83.0

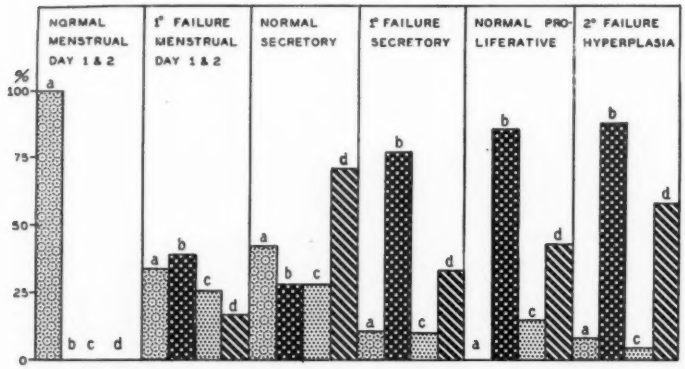

Chart 8. Chromatin granule distribution and mitosis in stroma nuclei of specimens of normal and abnormal endometrium. a, Percentage of specimens having diffuse, and b, percentage of specimens having aggregate chromatin in stroma nuclei. c, Percentage of specimens having intermediate type of chromatin in stroma nuclei. d, Percentage of specimens in group having mitotic figures in stroma.

short cycles (Chart 4). The first degree failure menstrual specimens secured after short cycles closely resembled the normal secretory tissues in gland chromatin characteristics, with the exception that the mitotic frequency was lower in the former group than in the normal secretory group (Chart 4, column 3; Chart 7, column 3). *Stromal nuclei.* The outstanding contrast between the groups of normal menstrual specimens and the 46 first degree failure menstrual specimens was the lower number of specimens containing the diffuse type of chromatin in the stromal nuclei, and the higher number of specimens with mitotic figures in the pathological tissues (Table V, Chart 5). It was interesting to note that although the group of first degree failure tissues after long cycles contained a number of specimens with the aggregate type of chromatin, there were no mitotic figures present in the stromal cells, and also there were no specimens of this group with the diffuse chromatin in the stroma (Table V, Chart 5). There were fewer of the solid "pycnotic" nuclei in the first degree failure menstrual specimens, than in the normal menstrual ones (Table V, Chart 6) and more of the granular nuclei which had smooth contours (in the pathological specimens) than there were in the normal tissues (Table V, Chart 6).

Normal secretory and first degree failure secretory tissues. Gland nuclei. Reference to Chart 7, columns 3 and 4 shows at once that the outstanding difference between the normal secretory and first degree failure secretory tissues was the greater number of specimens with mitotic figures in the group of normal

TABLE VII.—STROMAL NUCLEI IN NORMAL AND PATHOLOGICAL SPECIMENS OF ENDOMETRIUM

Tissue diagnosis	Tissue reaction	No. of specimens	Chromatin distribution in stromal nuclei—per cent			Nuclear form in stroma		Specimens having mitosis—per cent
			Diffuse	Aggregate	Intermediate	Av. % smooth nuclei	Av. % solid nuclei	
Normal	Menstrual	4	100.0	0.0	0.0	19.0	20.4	0.0
1° failure	Menstrual	46	34.8	39.1	26.1	24.9	13.4	17.0
Normal	Secretory	14	42.8	28.6	28.6	41.5	12.6	71.0
1° failure	Secretory	9	11.0	77.0	11.0	45.6	19.0	33.0
Normal	Proliferative	7	0.0	85.6	14.4	38.5	5.0	43.0
2° failure	Proliferative	24	8.3	87.5	4.1	61.5	7.7	58.0

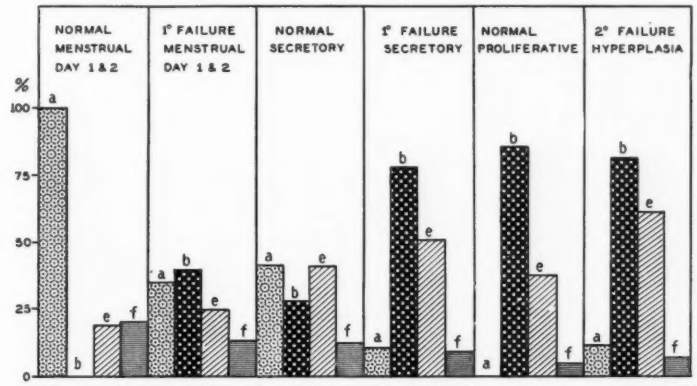

Chart 9. Stroma studies: chromatin granule distribution and per cent average of solid nuclei and granular nuclei with smooth contour in normal and abnormal specimens of endometrium. a, Percentage of specimens having diffuse and b, percentage of specimens having aggregate chromatin in stroma nuclei. e, Per cent average of granular nuclei with smooth contours in stroma of specimens in the group, based on cell counts. f, Per cent average of solid chromatin nuclei in stroma of specimens of group, based on cell counts.

tissues. *Stromal nuclei.* The stromal nuclei in the pathological specimens were predominantly of the aggregate type of granule distribution, although the number of specimens with mitotic figures in the first degree failure tissues was about half of that in the normal secretory tissues (Chart 8). In the pathological stroma there was a higher percentage of nuclei with smooth contour than in the normal secretory tissue (Table VII, Chart 9).

Normal proliferative tissues and hyperplastic endometrium. Gland epithelium. The aggregate type of chromatin predominated in normal proliferative tissues, the exceptions being due to the presence of the day 8 and 10 specimens, mentioned previously. Most of the normal specimens contained mitotic figures. The hyperplastic specimens uniformly had the aggregate type of chromatin in the gland nuclei and each contained mitotic figures (Table VI, Chart 7). *Stromal nuclei.* The stromal nuclei, in both the normal and pathological proliferative tissues, likewise exhibited the aggregate type of granule distribution in a large percentage of the cases (Table VII, Chart 8). There were fewer specimens with mitoses in the stroma than in the gland epithelium in both groups of tissues (Chart 8), although the hyperplastic group contained more specimens with mitoses than did the normal group. The number of nuclei with smooth contours was definitely greater in the stroma of the hyperplastic tissues than in the normal proliferative (Table VII, Chart 9). The averages of solid "pycnotic" nuclei were small in both groups of this tissue.

Normal tissues and specimens of bleeding endometrium. Table IX incorporates the data on 12 tissues secured from patients who were bleeding at the time the specimen was obtained, and had been doing so for the periods of time indicated in the first column of the table. This data has been included for comparison with that on normal tissues contained in Table VIII. The day 9 bleeding specimen resembled somewhat the day 8 and day 10 normal tissues in chromatin distribution in both glands and stroma, and the day 14 and day 23 bleeding tissues likewise resembled the day 14 and 23 normal tissues.

EVALUATION OF STUDY

The relation of the presence of aggregate granular chromatin to the presence of mitotic figures, especially in those tissues manifesting the characteristics generally attributed to proliferation in the endometrium and the fact that the follicular hormone is known to be responsible for these characteristics, suggests that the aggregate type of granular chromatin

distribution is associated with the presence of the follicular hormone. The more varied nuclear pictures encountered in the tissues secured during the secretory phase of the cycle may well be due to the simultaneous action of the corpus luteum and follicular hormones upon the endometrium, since there are fewer tissues with the aggregate type of chromatin in the secretory specimens, even though the number of these specimens containing mitotic figures is relatively high (Charts 7 and 8).

Certain points must not be lost sight of in evaluating the results herein described. The number and types of tissue included were such that no sweeping conclusions regarding endometrial modifications have been justified, and those conclusions tentatively advanced are based upon results obtained by grouping tissues with similar characteristics and averaging the occurrence of certain nuclear forms for comparison in the various groups. The information concerning mitosis may be misleading if the reader does not keep in mind that the presence of one mitotic figure, or of many such, entitled a specimen to be listed as manifesting mitotic activity, so that the figures on cell division are qualitative and not quantitative reports. The determination of the type of distribution of the chromatin granules contains a subjective element impossible to ignore, and the intergrades of distribution between a typical diffuse and a typical aggregate distribution of granules are often difficult to determine.[1]

The figures for the charts have been compiled by calculating the percentages of various factors occurring in each of the groups of tissue. For example, in Chart 2, column 2, 48 of the 52 specimens designated as proliferative in character, or 92 per cent of the tissues in that group, contained the aggregate type of chromatin in the gland epithelium, while 45 of the 52, or 86 per cent, of the specimens had at least 1 mitotic figure in the gland epithelium. In Table I, Chart 1, there were 56 specimens containing diffuse chromatin in the stroma, and the average of all the cell counts of solid "pycnotic" nuclei in the stroma of these 56 tissues was 27 per cent. There was an average of 6.6 per cent solid pycnotic nuclei in the stroma of the 99 tissues containing the aggregate chromatin in the stromal cells. Thus it is obvious that this study yields characteristics for groups of similar tissues, rather than specific characteristics of individual tissues.

Some elements of this investigation yield quantitative evidence for long established qualitative characteristics of endometrium from a physiological standpoint. This is apparent in regard to the proliferative action of the follicular hormone upon the endometrium, as well as to the difference between the gland and stromal cells in responding to hormonal stimuli. The threshold response of stromal tissues to hormonal stimulus is higher than that of the epithelial cells, hence the stromal response appears to lag (79, 82) behind that of the epithelial as the hormone level changes. The normal proliferative and hyperplastic tissues, almost uniformly containing aggregate chromatin and mitotic figures (Charts 7 and 8), histologically demonstrate the relation of the follicle hormone to tissue proliferation. This same group of tissues, in which there are more specimens with mitotic figures in the glands than there are with mitotic figures in the stroma, may well indicate the lag of the stroma in response to hormonal stimuli (Charts 7 and 8). This stromal lag is probably further demonstrated in the group of secretory tissues (both normal and first degree failure specimens) where there are more tissues containing aggregate chromatin and mitotic figures in the stroma than there are specimens with aggregate chromatin and mitotic figures in the gland epithelium, since the gland tissue during the secretory phase of the cycle is more concerned with the hormone of the corpus luteum than that of the follicle (Charts 7 and 8, columns 3 and 4).

This study has directed attention to the form of nuclei and their structure in the endo-

[1]As a matter of fact five, rather than three, grades of granule distribution were used in the original records; they were: (1) the typical diffuse; (2) the almost typical diffuse; (3) the typical aggregate; (4) the almost typical aggregate; and (5) the truly intermediate type which could not be considered as tending either toward a diffuse or an aggregate type of distribution. In computing the percentages of specimens having the diffuse or aggregate form of chromatin within the various groups of tissue, all specimens approximating the diffuse distribution were included with the typical diffuse specimens, and all those approximating the aggregate were included with the typical aggregate, in order to simplify the tables and charts.

TABLE VIII.—NORMAL SPECIMENS OF ENDOMETRIUM FROM NORMAL CYCLES

Day in cycle	Tissue number	Chromatin glands	Stromal nuclei			Tissue reaction	Length previous cycle	Length present cycle
			Types of granules	% smooth nuclei	% solid nuclei			
				Menstrual				
1	4446	Diffuse	Diffuse	16.9	11.5	Menstrual	34	34
2	4549	Diffuse	Diffuse	31.3	11.7	Menstrual	29	27
	4753	Intermediate	Diffuse	19.1	29.7	Menstrual	28	30
	4853	Diffuse	Diffuse	8.7	29.0	Menstrual	30	30
3	4899	Aggregate	Aggregate	47.0	2.8	Menstrual	28	33
				Postmenstrual and interval				
5	4906	Aggregate*	Aggregate	46.5	0.6	Postmenstrual	27	27
8	4659	Diffuse*	Diffuse	21.8	15.7	Interval	26	25
10	4912	Diffuse	Intermediate	11.9	16.8	Postmenstrual	28	33
11	4737	Aggregate*	Aggregate	30.2	1.3	Estrin	28	28
13	4683	Aggregate*	Aggregate*	52.2	0.6	Estrin	27	27
17	4929	Aggregate*	Aggregate*	60.0	0.6	Estrin	28	33
18	4755	Aggregate*	Aggregate*	47.5	0.0	Estrin	28	28
				Secretory				
14	4681	Diffuse*	Diffuse*	58.1	1.1	Early secretory	30	25
16	4798	Intermediate	Intermediate	4.3	70.0	Early secretory	28	30
18	4605	Diffuse*	Diffuse	49.6	1.1	Secretory	30	26
19	4695	Aggregate	Aggregate*	23.6	5.0	Secretory	27	27
22	4694	Diffuse*	Diffuse*	55.0	0.6	Secretory	30	27
23	4736	Diffuse*	Diffuse*	12.6	38.0	Secretory	30	29
24	4910	Intermediate	Intermediate	4.1	2.8	Secretory	30	30
25	4630	Diffuse*	Diffuse*	66.0	0.0	Secretory	30	26
	4776	Aggregate	Aggregate	45.6	7.1	Secretory	28	28
	4950	Intermediate*	Aggregate*	59.0	2.7	Secretory	28	33
26	4710	Diffuse*	Intermediate*	11.5	3.4	Secretory	27	27
27	4891	Diffuse	Diffuse*	41.2	1.9	Secretory	32	28
31	4964	Diffuse	Intermediate*	62.4	2.3	Secretory	28	33

*Mitotic figures present in tissue.

metrium which may prove of value in determining the normal and abnormal endocrine balances in the menstrual cycle. This idea appears feasible with reference to the lag reaction of stroma mentioned; the stroma, because of its higher threshold response, is more sensitive to hormone withdrawal than is the gland epithelium. Because of this difference in tissue response, it is entirely possible that the stroma may prove to be the tissue upon which the diagnoses of the earliest endocrine imbalances may be made. This concept is supported by the evident contrast of mitotic activity in the stroma of the normal secretory specimens and of the first degree failure secretory specimens (Chart 8). The number of specimens with mitotic figures is greater in the group of normal tissues, although there are few specimens with frank aggregate chromatin, than it is in the first degree failure specimens which predominantly have the aggregate chromatin in the nuclei of the stroma, but in only a few instances contain mitotic figures in this region (Chart 8, columns 3 and 4).

On the other hand, no such contrast exists between the stroma of first and second degree failure specimens of endometrium, for the only difference is in the number of specimens which contain mitotic figures. The contrast between

TABLE IX.—BLEEDING SPECIMENS OF TISSUE

Days elapsing since onset of bleeding	Tissue number	Chromatin glands	Stromal nuclei			Clinical diagnosis
			Type of granules	% smooth nuclei	% solid nuclei	
9	4701	Diffuse	Diffuse	0.0	80.2	Luteal menorrhagia
10	4936	Aggregate*	Aggregate	81.5	1.8	2° failure
12	4933A	Aggregate*	Aggregate*	11.9	5.8	2° failure
14	4724	Diffuse	Diffuse*	45.7	0.0	1° failure
17	4869	Aggregate*	Aggregate*	78.0	4.8	2° failure
21	4276	Aggregate*	Aggregate*	74.6	0.0	2° failure
23	4911	Diffuse	Diffuse*	24.9	1.8	
27	4885	Aggregate*	Aggregate*	96.3	0.0	2° failure
	4060	Aggregate*	Aggregate*	96.0	0.0	2° failure
28	4066	Aggregate*	Aggregate*	24.2	1.5	2° failure
	4137a	Intermediate	Intermediate*	11.4	3.7	1° failure
29	4898	Diffuse*	Diffuse	32.8	6.4	

*Mitotic figures in tissue.

these two types of tissue is found in the more sensitive gland epithelium which, in the partial failure of the corpus luteum hormone, reacts to the presence of diminished amounts of the factor after the stroma has ceased to show anything but the coarse chromatin characteristic of the follicular hormone effect (Charts 7 and 8, columns 4 and 6). It is possible that a differentiation between a severe first degree failure and a mild or early second degree failure of the ovarian hormones may be determined on the basis of the gland epithelium characteristics with respect to the chromatin form in the nuclei.

Furthermore, if the concept of stromal lag to hormone stimulation is basically sound, and if normal and first degree failure endometrium may be differentiated on the basis of stromal changes, and first and second degree failures on the basis of epithelial modifications, then it is plausible to suppose that the earliest manifestations of a complete failure of both ovarian hormones should appear in the stroma. This prediction is based on the theory that the epithelium will continue to respond to diminished amounts of the follicular hormone after the stroma has ceased to do so. Schroeder (78) makes the statement that stromal changes appear first in pathological endometrium and that glandular changes appear secondarily.

The waves of pycnosis usually ascribed to the stroma of menstrual tissues are apparently not limited entirely to these specimens, since they have been observed in tissues secured during the first few days of each of the following weeks of the cycle, i.e., days 8 to 10, 16, and 23.[1] That the pycnosis is not necessarily a true pycnosis indicating cell death is evidenced by the relatively high percentage of these nuclei in tissue number 4912 and their absence in tissue number 4929, both tissues having been obtained from the same individual within the same cycle (Table VIII). Furthermore, these "pycnotic" nuclei lack the rounded condensed form of the necrotic nucleus and have, instead, an irregular shape resembling that characteristic for the nuclei in the stroma of the basalis. It has been suggested[2] that the form of the chromatin in the basalis of the endometrium is the result of a poor capillary blood supply, and it may be that the appearance of nuclei showing similar characteristics in the functional layers is due to modifications of the capillary bed in these areas. It has been shown that the capillary bed is quite sensitive to variations in the follicular hormone content of the blood in the work of Markee (66, 66a) on intra-ocular endometrial transplants in castrate animals.

Should the waves of "pycnosis" in the functional layers of the endometrium be

[1] Schroeder (78) reported rod cells in the gland epithelium throughout the cycle; Keller and Schickele (56) reported pycnosis in a day 16 specimen, and Buettner (18) reported pycnosis on days 13, 17, and 20.

[2] Personal communication from Dr. E. W. Goodpasture, Department of Pathology.

shown to be due to vascular phenomena dependent upon fluctuations in the follicular hormone content of the blood, then these waves of pycnosis would afford histological evidence of weekly variations in the production of the follicular hormone (Table VIII); such weekly fluctuations in the excretion of the follicular factor, whether in free or combined form, are indicated in the charts in the literature on follicular hormone excretion (42, 46, 85, 86), while a lessening of mitotic activity has been reported in specimens of endometrium secured on days 9 (56), 10 (50), 14 (56), 16 (77), and 23 (56).

SUMMARY

A study of 200 specimens of human endometrium, obtained from normal women and from women exhibiting various degrees of ovarian failure, revealed that two forms of nuclei can be distinguished, namely, a granular and a non-granular or solid homogeneous form. Further, the granular form of nucleus showed two distinct types of chromatin distribution, aggregate and diffuse. The aggregate type of granule distribution appeared almost uniformly in the nuclei of endometrial specimens diagnosed as presenting the characteristics of proliferation, but was not predominant in the secretory or menstrual tissues.

Hence the conclusion seems justified that the aggregate type of chromatin distribution is characteristic of human endometrium which is under the influence of the follicular hormone alone (normal proliferative phase, second degree ovarian failure). As a whole, tissue from women with first degree ovarian failure showed the aggregate type of chromatin in the stroma more frequently than did tissue obtained from normal women during the secretory and menstrual phases. On the other hand, the gland chromatin in tissue associated with first degree ovarian failure showed no significant differences from that of the normal. These observations suggest that differences in the threshold response of the gland and stromal nuclei of the human endometrium to hormonal stimulation may furnish a basis for determining fluctuations in endocrine levels.

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PAPILLARY TUMORS OF THYROID AND LATERAL ABERRANT THYROID ORIGIN

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ALTHOUGH any study of tumors of the thyroid is rendered difficult by the multitude of different classifications that have appeared in the literature, the papillary tumors form a fairly distinct group. This group includes the papillary adenoma and the papillary carcinoma. Papillary tumors, either benign or malignant, may originate in the thyroid gland proper, in lateral aberrant thyroid tissue, or they may co-exist in both the thyroid and the lateral cervical regions. The papillary carcinomas constitute 17.7 per cent of all carcinomas of the thyroid in the Cleveland Clinic series.

PAPILLARY TUMORS OF THE THYROID GLAND

In the present discussion of papillary tumors only those tumors 2 centimeters or more in diameter are considered. Therefore, when we refer to a papillary adenoma or carcinoma of the thyroid, this can be taken to mean a gross tumor of clinical importance.

As Graham (14, 15) has repeatedly stated, the various groups of neoplastic lesions of the thyroid blend almost indiscernibly into one another. In a series of malignant tumors of the thyroid gland he says, "We find all grades of transition of the original adenoma into all types and combinations of morphological cancer mentioned in the literature, except pure papilliferous adenocarcinoma and pure scirrhous carcinoma. These various combinations of adenoma and morphological cancer are present in the series of tumors and frequently in a single tumor."

The difficulty encountered in classifying carcinomas of the thyroid is often increased by the finding of one type of cellular arrangement in one part of the tumor and quite a different arrangement in another part of the same tumor. Thus a malignant adenoma, in which the tumor is invading the blood vessels, may in one section show a medullary arrangement and in another a well differentiated papillary structure. Therefore, in the group under consideration we have eliminated all cases of papillary carcinoma in which there were present medullary areas with invasion of blood vessels by the tumor. A tumor which shows invasion of the blood vessels is here classified as a malignant adenoma even though it contains papillary areas.[1]

The tumors included in this study are divided into 3 groups. First, the papillary adenomas which are considered to be benign from a histological standpoint (15 cases); second, those which either as a result of invasion of the capsule or the appearance of the cells were considered to be malignant (20 cases); and lastly, the tumors arising in lateral aberrant thyroid tissue (13 cases).

Although it is not so difficult to set off the group of pure papillary tumors from other adenomas and carcinomas of the thyroid, it is extremely difficult from a histological standpoint to differentiate between the benign and malignant papillary tumors. No two pathologists would agree as to which tumors in this group were benign and which malignant. This is not surprising when the subsequent course is reviewed and it is found that in certain cases in which the tumor was apparently incompletely removed and in which the histological appearance of the tumor suggested carcinoma, the patients are alive without evidence of recurrence 5 years or more after operation. It is equally significant to note that in *no instance have we observed either distant or regional metastases from papillary tumors which did not show tumor cells within blood vessels.*

Only 5 of the 35 patients with papillary tumors of the thyroid have died as a result of

From the Cleveland Clinic.

[1]Invasion of blood vessels is rarely seen in tumors that are predominantly papillary. It was necessary to reclassify only 3 papillary carcinomas because of the finding of blood vessel invasion by tumor tissue.

the tumor. In 1 case a biopsy was performed and death occurred a year later. No information as to the exact cause of death can be obtained. In the second case a fatal hemorrhage occurred a month after the tumor was treated with radium, probably a result of slough secondary to the irradiation. In the third, fourth, and fifth cases local recurrences of incompletely removed tumors were responsible for the patients' deaths 7 months, 16 months, and 3 years, respectively, after the operations had been performed.

In 5 instances the patients are alive and well from 2 to 11 years after what appeared to be an *incomplete* removal of tumors classified as papillary carcinomas. Radiation therapy was given in 4 of these 5 cases, but in 1 case the patient has remained alive and well 11 years without radiation therapy. In this case, examination of the gross specimen showed that the tumor appeared to have been incompletely removed.

In addition to these 35 cases of papillary tumors of the thyroid itself, we have observed 13 cases of papillary tumors arising in lateral aberrant thyroid tissue. In 5 of these 13 cases the thyroid gland has contained papillary tumors similar to the tumors in the lateral cervical region. In 3 cases the thyroid tumor was believed to be malignant yet no patient has died as the result of the disease. In no instance has distant metastasis occurred and in no instance have we any proof that the lateral nodules are metastases rather than multiple primary tumors.

In short, it would appear that the papillary group of tumors of thyroid and lateral aberrant thyroid origin are remarkably benign, do not tend to metastasize, and if completely removed will not recur. Even an apparently incomplete removal has been followed in 1 instance by no recurrence over a 4 year period. It is, therefore, questionable whether these tumors are true carcinomas or whether they should be classified as only "locally" malignant as are the mixed tumors of the salivary glands.[2]

[2]Of the 3 cases formerly classified as papillary carcinoma, but eliminated from this series because of demonstrable invasion of veins, 2 patients are alive and without evidence of recurrence 2 years and 7 years, respectively, after operation, and the third died of skeletal metastases 5 years after operation.

TUMORS OF LATERAL ABERRANT THYROID ORIGIN

Literature. In 1932, Moritz and Bayless reported 6 tumors of lateral aberrant thyroid origin and collected 103 cases from the literature. Since that time 26 additional cases have been reported making a total of 135 cases. Moritz and Bayless classified 31 of their collected cases as malignant and since their report this number has been increased to 45.

Only 2 of the 45 patients with malignant tumors of lateral aberrant thyroid origin have been reported to have died as a result of recurrence of the tumor following operation. In no case has either local or distant metastasis of the tumors been proved. The remarkable survival record of these patients cannot fail to raise the question of whether or not the tumors in question are really malignant.

The strongest advocate of the malignancy of lateral aberrant thyroid tumors has been Dunhill who reported 4 cases, 2 of which he was unable to trace more than 3 years after operation. In the third case a local recurrence developed and the patient died without evidence of distant metastasis 9 months after operation. The fourth patient died as a result of intestinal obstruction secondary to a pelvic malignancy, the type of malignancy having apparently never been determined. The only deduction that can be drawn from this group of cases is that tumors of lateral aberrant thyroid origin may recur locally if they are not completely removed.

Many of the tumors in the collected series were described as showing extensive metastasis to the cervical lymph nodes. Similarly it has repeatedly been stated in the literature (8, 31) that metastasis to the regional lymph nodes is commonly associated with papillary carcinoma of the thyroid.

In our experience, papillary tumors of the thyroid have not metastasized to lymph nodes. Recently it has been recognized (6) that, in the presence of lateral aberrant thyroid tumors, the thyroid gland is apt to contain co-incidentally 1 or more papillary tumors similar to those in the lateral cervical regions. It is, therefore, clear that it is difficult to differentiate between (1) a papillary adenoma of the thyroid associated with

multiple papillary adenomas of lateral aberrant thyroid origin, and (2) a papillary carcinoma with metastasis to the cervical nodes. Histologically there is little to differentiate the two.

Lymphoid tissue tends to be present in all lateral cervical sinuses, cysts, and other embryological anomalies of the neck. Lateral aberrant thyroid tumors are no exception to this rule as they also tend to contain considerable lymphoid tissue and may have the histological appearance of a lymph node containing metastatic carcinoma (Fig. 1). In short the final answer to the question as to whether these tumors are benign primary tumors or metastatic carcinoma must be decided by the clinical course of the tumor and the survival of the patient. Since there is no case either in our series or in the literature in which the tumor has continued to disseminate itself after operation and has thereby caused the death of the patient, it would appear that these tumors are essentially benign and should not be classified as metastasizing carcinomas of the thyroid.

Clinical material. In the past 15 years, 13 patients with tumors arising in lateral aberrant thyroid tissue have been seen at the Cleveland Clinic. By some freak of distribution I have operated upon 6 of these in the last 2 years. Four cases in this group are of particular interest from both clinical and pathological standpoints, not only because of the extensiveness of the involvement, but also because of the difficulties involved in interpreting the histology of the tumors.

CASE 1. The patient was a married woman, 27 years of age, who complained of a painless lump in the posterior triangle of the neck just above the clavicle. The enlargement was noted during a pregnancy. Examination showed a slight, firm enlargement of the left lobe of the thyroid, multiple soft movable tumors in the posterior triangle on the left, and several small soft nodules deep to the sternomastoid on the right. A clinical diagnosis of tuberculous glands, possibly lateral aberrant thyroid, was made and one of the nodules was removed for microscopic examination.

The nodules were found to be papillary adenomas arising in lateral aberrant thyroid tissue and their removal was advised. At the time of operation, 25 separate nodules were dissected out of the neck and the left lobe of the thyroid was completely removed.

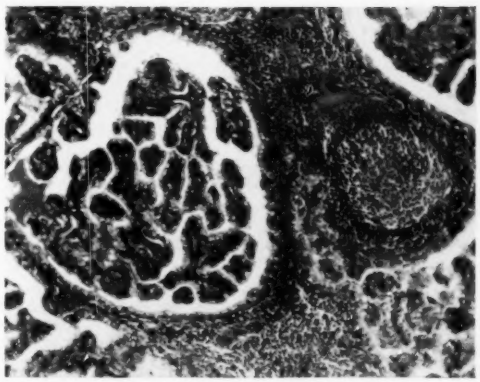

Fig. 1. Photomicrograph of lateral aberrant thyroid nodule showing large amount of lymphoid tissue closely associated with the epithelial elements. (Case 2.)

This lobe showed a diffuse papillomatosis extending medially nearly to the isthmus. The lateral nodules were encapsulated but some of them were quite adherent. Those close to the trachea and the left lobe of the thyroid were particularly adherent and appeared to be involved in a diffuse inflammatory process which plastered them to the trachea and to one another in firm masses. This reaction was the result of degeneration and calcification of the tumors. The patient is well 1 year after operation (Figs. 2, 3, and 4).

CASE 2. The next case is strikingly similar to the one just reported. The patient was also a woman 27 years of age whose complaint was a painless lump in the neck. Examination showed multiple, soft, movable nodules behind the sternomastoid on the right and a hard tumor in the right lobe of the thyroid. A diagnosis of papillary adenoma of the thyroid and multiple papillary adenomas in lateral aberrant thyroid tissues was made. A block dissection of the neck was performed leaving the sternomastoid muscle but taking the jugular vein and the entire right lobe of the thyroid. There were 17 tumor nodules in all, distributed almost exactly as in Case 1. All were papillary adenomas and there was also a papillary adenoma in the right lobe of the thyroid. It is now more than 1 year since the operation and the patient is well and has no evidence of recurrence.

In the last 2 cases the tumors were clearly benign from both the clinical and histological points of view. In the following cases malignancy is more difficult to exclude:

CASE 3. The patient was a woman 45 years of age who was first seen in the Clinic in 1929, complaining of a gradually enlarging mass in the neck. Examination showed a firm, nodular goiter. At the time of

Fig. 2. Drawing to show distribution of lateral aberrant thyroid nodules. (Case 1.)

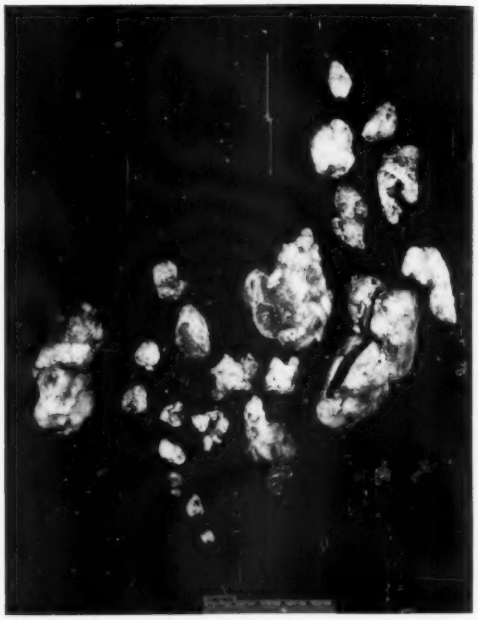

Fig. 3. Photograph of lateral aberrant thyroid nodules. (Case 1.)

operation it was found that the left lobe of the thyroid contained a hard tumor and a number of small nodules were palpable beneath the sternomastoid muscle. A subtotal thyroidectomy was performed by Dr. A. T. Bunts and 4 nodules were excised. A diagnosis of papillary adenoma of the thyroid (? malignant) was made and the nodules were interpreted as papillary adenomas arising in lateral aberrant thyroid tissue. The patient was given 2,800 roentgen units to the neck and has remained well for 9 years with no evidence of recurrence. If these tumors had been the result of metastasis from a papillary carcinoma of the thyroid, I am certain that simple excision of 7 metastatic nodules followed by 2,800 roentgen units would not have cured the disease.

CASE 4. The patient was a man 40 years of age who had noticed a gradually enlarging, painless lump in his neck for 1 year prior to entry. Examination showed several firm, movable nodules lying behind the sternomastoid muscle and a hard tumor in the right lobe of the thyroid. A diagnosis of papillary adenoma of the thyroid and lateral aberrant thyroid tumors was made. Six nodules were removed and a radical resection of the entire right lobe of the thyroid was performed. The pathologist's diagnosis was malignant adenoma of the thyroid and multiple malignant adenomas arising in lateral aberrant thyroid tissue. There was definite invasion of the capsule of the thyroid tumor and tumor cells were growing in blood vessels (Fig. 5).

Several months later the patient returned with a recurrent nodule which was palpable in the right side of the neck beneath the sternomastoid. At operation the sternomastoid muscle, the jugular vein, and all the tumor-bearing tissues of the right side of the neck were removed. Nine more nodules (making 15 in all) were present in this tissue, one being removed from behind the carotid artery and vagus nerve and several from the superior mediastinum. The patient is well 18 months after the first operation and there is no evidence of recurrence or distant metastasis.

The malignant qualities of the tumor, as shown by its invasion of the capsule and the blood vessels, raises the question of whether the nodules in the neck were metastases from the malignant adenoma in the thyroid. We know, however, that malignant adenomas of the thyroid rarely metastasize by the lymphatics but tend rather to spread through the blood stream to the lungs. It is quite possible that distant metastasis may occur or that the nodules already removed were actual metastases from the thyroid tumor, but their dis-

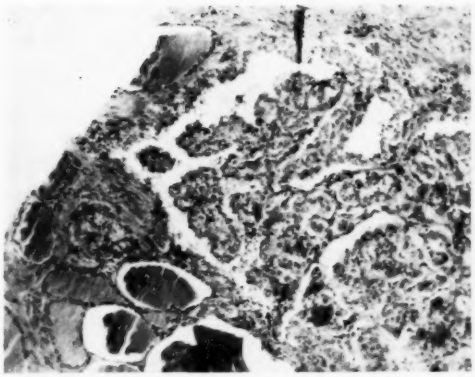

Fig. 4. Illustration of section of left lobe of the thyroid showing diffuse papillary adenomatosis of the major portion of the entire lobe. (Case 1.)

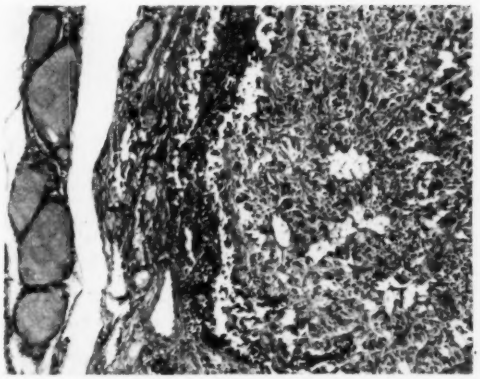

Fig. 5. Photomicrograph of malignant adenoma of the thyroid, showing definite invasive qualities. The lateral cervical tumors showed a similar structure. (Case 4.)

tribution was so similar to that of the nodules in the other cases, and metastasis to the regional lymph nodes is so rarely seen in malignant adenomas of the thyroid, that I believe each tumor is a primary malignant adenoma arising in lateral aberrant thyroid tissue.

Age. The ages of the 13 patients in this series varied from 18 to 56, the average age being 34 years. Forty-six per cent of the patients were between 20 and 30 years of age.

Sex. Tumors arising in lateral aberrant thyroid tissue are much more common in women than in men, the ratio being 12 to 1 in this series. In 1 case the tumor was first noticed during a pregnancy.

Race. Six of the 13 patients in this series and 4 of the 6 patients with extensive multiple tumors were of Jewish extraction.

Symptoms. A painless lump which either enlarged very slowly or not at all was the most common symptom. In 23 per cent of the cases, however, the patient had not noticed the tumor and it was discovered only during examination or operation for a goiter. In only 15 per cent of the cases was the mass either painful or tender. The duration of the symptoms varied from 1 week to 5 years and averaged 15 months.

Examination. The consistency of the lumps was usually described as being either soft or firm and the nodules were generally considered to be lymph nodes. The extensiveness of the distribution of the nodules was rarely apparent from external examination, their soft consistency and their location deep beneath the sternomastoid rendering them very difficult to palpate. In the cases with multiple tumors in which the thyroid was similarly involved, the affected lobe was hard and suggested the presence of either a thyroiditis or a malignancy.

Distribution of nodules. The lateral aberrant thyroid tissue was found in all triangles of the neck. In 6 cases the nodules were on the left, in 4 cases on the right, and in the remaining 3 cases they were bilateral. In 1 of the bilateral cases, however, there were multiple nodules on one side and only a single nodule on the other. In Cases 11 and 13 there was extensive bilateral distribution of the tumors. It should be noted that in all cases having more than 6 lateral aberrant thyroid nodules, 1 lobe of the thyroid was involved in a similar pathological process. In 4 of these 6 cases the tumors were present in the superior mediastinum. The nodules were also found posterior to the trachea and posterior to the carotid sheath.

Number of nodules. The number of nodules varied from 1 to 25, averaging 7. In 4 cases only 1 nodule was found and in 6 cases there were 6 or more separate tumors. In the case in which 25 nodules were present the actual count could be increased to 30 or more by separating tumors which were adherent to one another but were removed in a single mass.

Thyroid gland. Two of the 13 patients had colloid adenomatous goiters without hyperthyroidism and 1 gave a history of having had treatment for an adolescent goiter. In 6 cases (all in patients with 6 or more lateral aberrant nodules) it was found that the same process was going on in the lobe of the thyroid on the affected side as in the lateral aberrant tissue.

The findings were as follows: adenopapillomatosis, 2 cases; benign papillary adenoma, 1 case; papillary adenoma (malignant?), 1 case; malignant adenoma (no papillary structure), 1 case; and nodule palpable in thyroid (patient refused operation), 1 case. In only 5 cases was the thyroid normal.

Histology of lateral aberrant thyroid tissue. In 5 cases the lateral aberrant thyroid tissue was found to be composed of cystic papillary adenomas. Solid papillary adenomas were present in 5 cases. In 1 case the tumors were papillary adenomas (malignant?), in 1 case the tumors were interpreted as frankly malignant papillary adenomas, and in 1 case they were malignant adenomas with no papillary structure. In this case each of the 17 tumors was apparently an independent malignant adenoma with structure similar to the malignant adenoma in the lobe of the thyroid. An iodine determination done on the lateral aberrant thyroid tissue in case 13 showed 3.4 micrograms of iodine per 100 milligrams of tissue.

Previous treatment. In 4 cases roentgen therapy was given before operation without any change in the size of the nodules. In 1 of these cases a biopsy taken at another hospital was reported to have shown metastatic carcinoma. The roentgen therapy failed to produce any degenerative changes in the tumor, did not diminish the size of the nodules, and did not prevent the appearance of additional nodules which were later excised.

Diagnosis. In only 3 of the 13 cases was the correct diagnosis made before operation. In a fourth case the presence of lateral aberrant thyroid tumors was considered, but the diagnosis of tuberculous glands of the neck was preferred. In all the cases in which the correct diagnosis was made, there were 6 or more nodules in the neck and the lobe of the thyroid on the affected side was involved.

The distribution and consistency of the nodules usually suggest that they are lymph nodes. The pre-operative diagnoses in the 13 cases were: tuberculous glands, 4; lateral aberrant thyroid, 3; branchial cleft cyst, 2; nodules unsuspected until operation (thyroidectomy), 2; lymphoma, 1; abscess, 1.

At the time of operation the nodules were usually recognized as lateral aberrant thyroid tissue. When cystic, there is a characteristic bluish discoloration similar to that of a cystic adenoma of the thyroid. When solid they are of a reddish color and resemble thyroid tissue.

The characteristic feature that differentiates these tumors from lymph nodes is their vascularity and the presence of clearly visible blood vessels in the capsule. In some cases the tumors are adherent to one another and to surrounding structures and may be either calcified or surrounded with thick hyaline or fibrous capsules. These changes occur only when there is degeneration within the tumor and tend to be most marked in the nodules near the trachea.

In this series of 13 cases the tumors of lateral aberrant thyroid origin can be roughly divided into 2 groups. There is first, the group of 4 cases in which palpation and exploration reveal a normal thyroid and only 1 lateral tumor; and second, the group in which more than 6 tumors are present and 1 lobe of the thyroid is similarly involved. In the multiple group, when the thyroid is involved, nothing short of a radical resection of the affected lobe of the thyroid and a thorough exploration of the neck with removal of all nodules has effected a permanent cure. Four of the 6 patients in this group have each been subjected to from 2 to 4 operations because the extent of the involvement was not at first appreciated and complete excision of all tumors was not carried out.

End-results. Two of the 13 cases in this series have not been traced since operation. None of the 11 remaining patients, all of whom have been followed for periods varying from 4 months to 13 years (an average of over 4 years) has died as a result of thyroid or lateral aberrant thyroid disease, and at the present time no patient is known to be suffer-

ing any disability as a result of recurrence. Only 2 patients received deep roentgen therapy after operation.

One of the patients in this series had 2 nodules palpable prior to operation. Only 1 of these (a papillary adenoma) was removed, yet the patient has lived 13 years since operation and the remaining nodule has not enlarged or produced any symptoms. In Case 13, interpreted as a malignant papillary adenoma arising in the lateral aberrant thyroid, the patient is well and has no evidence of recurrence 4 years after operation in spite of the fact that the growth was invasive and was not completely removed. This patient was given 3,400 roentgen units to the affected side of the neck. A third patient had her first 2 operations elsewhere and has had 2 subsequent operations for benign cystic papillary adenomas. At least 6 nodules in all have been removed and now 5 years after the original operation, a nodule is palpable in the right lobe of the thyroid. This was one of our earlier cases and the thyroid itself was not explored at the time of operation. The nodule now palpable is in all probability a papillary adenoma of the thyroid.

In 2 of the remaining cases, recurrences have been excised. The recurrences appeared 2 months after the original operation in 1 case and 8 months after the original operation in the other. In both instances the recurrent nodules were widely distributed and doubtless represented tumors which were so small at the time of the first operation that they escaped detection. To date, therefore, in a series of 13 cases, 4 patients have had proved recurrences all of which have been controlled by a second operation.

Roentgen therapy. Four of the 13 patients in this series received roentgen therapy before operation. In none of these cases was there any appreciable diminution in the size of the nodules nor did the roentgen therapy effect any histological changes or bring about any evidences of degeneration. In 1 case the growth of the tumor continued after 4,000 roentgen units and there was a recurrence of the nodules 8 months after the first operation.

In 2 instances roentgen therapy was given after operation. In 1 of these cases it would appear that the x-ray had held the tumor in check. But similar experiences with other cases in which roentgen therapy was not given cannot fail to suggest that the result might have been the same had no roentgen therapy been used.

Tumors arising in lateral aberrant thyroid tissue grow slowly, are well differentiated, and often seem capable of lying dormant for many years. From their highly differentiated histological appearance it is difficult to see how they could respond to roentgen therapy. Their clinical behavior makes it difficult to evaluate the results of irradiation. Since permanent cure has been effected in all patients subjected to surgery alone I can see no indication for adding roentgen therapy to surgery in the treatment of lateral aberrant thyroid tumors that have been cleanly excised.

Additional cases. There are 2 additional cases that are difficult to classify, the operating notes and pathological reports containing certain inconsistencies which make it impossible to be certain that the tumor was removed from the lateral cervical region. In 1 case, "lobulated, highly differentiated, colloid thyroid tissue" was reported in the wall of a cyst. Clinically, this cyst was described as being in the midline, but at the time of operation an apparent attachment of the cyst to the lateral pharyngeal wall was said to be present. In the second case, in the course of a thyroidectomy a "well differentiated colloid adenoma" was said by the pathologist to have been removed from the lateral cervical region. No mention of this piece of tissue was made in the operating note.

It is interesting to note that neither of these specimens shows any histological evidence of papillary structure or of malignant change. These are the only 2 specimens in this group of lateral aberrant thyroid tumors which fail to show either of these qualities.

Moritz and Bayless have reported 2 cases in which tumors, apparently removed from the lateral cervical region and not connected with the thyroid, were found to contain colloid adenomatous thyroid tissue without papillary structure.

In all of Cattell's 13 cases, however, and in the majority of other recently reported tu-

mors of lateral aberrant thyroid origin, the papillary structure is a constant finding. Tumors arising from the median anlage and thyroglossal tract, however, do not have this tendency to papillary structure. I am inclined, therefore, to believe that the first of these cases is a thyroglossal tumor and the second merely an adenoma shelled out of the thyroid gland.

CONCLUSIONS

Papillary tumors arising in thyroid and in lateral aberrant thyroid tissue are remarkably benign. The clinical behavior of these tumors, whether they are located in the thyroid proper or in the lateral cervical region, is so similar that a common embryological origin must be suspected.

If these papillary tumors are completely removed, they do not tend to metastasize or to recur locally. If a local recurrence should follow an incomplete operation, re-operation rather than palliation with roentgen therapy is advisable. When a papillary tumor is present in the thyroid and multiple nodules of the same histological structure are present in the lateral cervical region, these nodules should not be interpreted as incurable metastases from a carcinoma but should be considered as multiple benign tumors and should be removed. Likewise, when lateral aberrant thyroid tumors are found, the thyroid should be explored to rule out the presence of a similar type of tumor. It is my belief that many cases reported in the literature as papillary carcinomas of the thyroid with metastasis to the regional lymph glands are in reality benign tumors of lateral aberrant thyroid origin with a co-existent tumor in the thyroid gland itself.

Roentgen therapy has not been proved to be of value in the treatment of papillary tumors of thyroid and lateral aberrant thyroid origin. Reliance must, therefore, be placed upon the complete removal of these tumors by surgery. What may at first seem to be a hopelessly extensive carcinoma with multiple metastasis is often permanently cured by a persistent surgical attack. Despite the extensiveness of many of these operations, no deaths have occurred in the hospital following operation.

SUMMARY

1. Twenty cases of papillary carcinomas of the thyroid, 15 cases of papillary adenomas of the thyroid, and 13 cases of papillary tumors arising in lateral aberrant thyroid tissue are reported.

2. In only 5 of the 20 cases of papillary carcinoma of the thyroid has death occurred as a result of the tumor.

3. In no instance has it been proved that either regional or distant metastasis took place.

4. In nearly half the cases of lateral aberrant thyroid disease the lobe of the thyroid on the affected side contained a tumor histologically identical with the lateral cervical nodules.

5. It is often difficult to distinguish between multiple lateral aberrant thyroid tumors and metastatic papillary carcinoma in cervical lymph nodes.

6. It is probable that many cases reported as papillary carcinoma of the thyroid with metastasis to the regional lymphatics are in reality benign papillary lateral aberrant thyroids with a co-existent benign tumor in the thyroid gland.

7. Tumors arising in lateral aberrant thyroid tissue are essentially benign. Only 2 of the 45 patients classified in the literature as having malignant tumors of lateral aberrant thyroid origin have been reported to have died as a result of recurrence of the tumor following operation. None of the 13 patients in this series has died as a result of lateral aberrant thyroid disease.

8. It has not been proved that either distant or local metastasis occurs from papillary tumors of lateral aberrant thyroid origin.

9. Surgery is the treatment of choice for all papillary tumors of thyroid and lateral aberrant thyroid origin. Roentgen therapy has not proved effective in their treatment.

I wish to express my indebtedness to Dr. Allen Graham for his aid in the interpretation of the histology of the tumors reported in this paper.

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CYSTIC HYGROMA OF THE NECK

Report of Twenty-Seven Cases

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HYGROMA of the neck is an uncommon, endothelial lined, cystic lesion of lymphatic origin which is encountered most often in infancy and childhood. Individual reports of this condition have appeared from time to time in the medical literature, but few authors have had the opportunity to study many of these patients. We are, therefore, prompted to publish our experiences with 27 such cases which constitute a larger group than ever reported from one clinic. According to Dowd the first report was made by Redenbacher in 1828. The name congenital cystic hygroma was first employed by Adolph Wernher in 1843. For a résumé of the earliest publications the table compiled by Farr in Dowd's paper is worthy of note. The literature on this subject has been reviewed on several previous occasions. Dowd collected 91 cases which had been published prior to 1913. Vaughn added to this review, collecting all cases up to 1934, bringing the total to 155. Goetsch, in 1938, made an excellent pathological study of 12 personally observed cases. Adding a few isolated examples since the publications of Vaughn and Goetsch and including our own 27 patients, approximately 225 cases have been reported to date.

Cystic hygromas have been described in other regions of the body, particularly in the axilla and chest wall and less frequently in the groin. The cervical lesions, however, are much more common and constitute probably four-fifths of all hygromas which have been studied.

CLINICAL DATA

Cystic hygromas may arise in many regions of the neck. They tend to occur most frequently in the posterior triangle, lying behind the sternomastoid muscle, occupying the supraclavicular fossa (Fig. 12) or extending over toward the crest of the shoulder (Figs. 1 and 3). In a much smaller proportion of cases the cyst may occupy the anterior cervical triangle; but when it does so, there is a tendency for it to lie in a high position just beneath the angle of the jaw (Figs. 11 and 17) or to overlay the ramus of the mandible (Fig. 13). In Case 8 the cyst occupied a very high position and there was a projection into the floor of the mouth on the homolateral side. In a few striking examples of the condition, a massive cystic structure may completely fill the lateral hollow of the neck and extend from the side of the head well down to the tip of the shoulder (Fig. 1), and it may even bulge to the subclavicular fossa and axilla anteriorly and to the spine of the scapula posteriorly. In 17 of our patients the swelling was on the left side and in the remaining 10 the right side was involved.

The size of the mass does not bear any definite relationship to the age of the patient or to the duration of the lesion. Indeed, we have encountered some of our largest specimens in infants only a few weeks of age. The smallest cyst in our series is about 5 centimeters in length and 4 centimeters in diameter. Commonly they are described as "lemon" sized, less often they are "orange" sized, and occasionally the mass is large enough to efface the normal contour of the neck on the affected side. When the lesion is small, there appears to be only a single mass with a smooth, well rounded external contour; but in the larger growths a faintly lobulated surface indicates multilocular development. The cyst is usually not tense, and it commonly has a limpid consistency and poorly defined borders. While the overlying skin is essentially normal in

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texture, it may vary somewhat from its usual pinkish color and have a slightly bluish cast imparted to it by the underlying fluid. The thinness of the cyst wall and the clear colorless nature of the entrapped fluid permit the mass to be easily transilluminated. This latter finding is made in all of our cases excepting one in which there had been hemorrhage into the cyst cavity.

The local swelling is usually noted early in life. In our series 55 per cent were noted at birth, 75 per cent were discovered within the first year, and 90 per cent were present by the end of the second year. The oldest age in which we have seen initial development of the swelling was 14 years. However, Hyatt, Goetsch, and others have cited instances with onset of symptoms in adult life.

Males and females are affected in about the same proportions in previously tabulated cases, but in our series there is a higher incidence in the males in the proportion of 16 to 11. Reference has been made in the literature to the tendency of the tumor to occur in the first born child of a family, but in 16 of our patients, in whom there are statements regarding the siblings, only 3 were first born children.

Our patients were in the following age groups: 2 were in the first month of life; 7 were 1 to 6 months of age; 2 were 6 to 12 months of age; 7 were 1 year of age; 2 were 2 years old; 3 were 4 and 6 years old; and 1 was 19 years old.

Fig. 1. Case 2. Eight day old infant. Cystic hygroma of the neck which was present at birth.

X-ray examination of the cervical mass lends little additional information of value in most cases. The soft tissue swelling shows a shadow of rather uniform density with poorly defined borders (Figs. 2 and 14). The exact extent of the cavities can be demonstrated better by the injection of iodized oil, or better still an iodide solution, into the cyst as suggested by MacGuire and Vaughn. Roentgenological examination may aid in showing lateral displacement of the trachea or forward displacement of the upper esophagus. The most

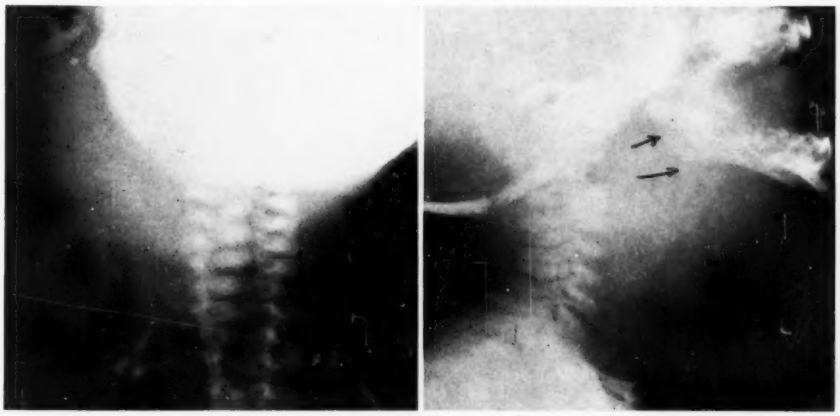


Fig. 2. Case 2. Anteroposterior and lateral roentgenograms of cervical hygroma. Compare with Figure 1. There is no lateral displacement of the larynx or trachea, but the posterior pharyngeal wall (indicated by arrows) is pushed forward.

a b c d

Fig. 3. Case 3. a and b, Pre-operative photographs. Five weeks old infant. Hygroma of the neck first noticed at birth. c, Wound 8 days after surgical excision of hygroma. The skin is loose and wrinkled, but during the course of subsequent weeks this redundancy spontaneously disappeared and a normal contour of the neck was re-established. d, Same patient 6 years after operation showing normal contour of neck.

important use of roentgenological study is to determine the presence of mediastinal involvement which, of course, would have considerable bearing on the type of therapy to be instituted.

PATHOLOGY

Macroscopic findings. The hygromatous cyst, when removed from the neck, is a rounded, ovoid, or smoothly lobulated sac (Figs. 4 and 8) which is thin-walled and translucent. The paper thinness of the walls and the fluid content of the sac impart to the specimen a soft consistency. The structure is usually monolocular, but there may be side pockets separated by fibrous septa which freely communicate with the main cavity (Fig. 15). Thus, the puncture of any one of the accessory chambers results in a collapse of the entire specimen. One rarely encounters a group of closely adherent thin walled cysts which do not possess openings between their lumina, but in one case (Fig. 18) we have seen this form of the lesion. The walls of the cysts have a very low vascularity, and the blood vessels which are present are always quite

Fig. 4. Case 3. Photograph of surgically removed cystic hygroma. The cyst is thin-walled and is slightly lobulated. The elliptical structure toward the left is an included portion of skin.

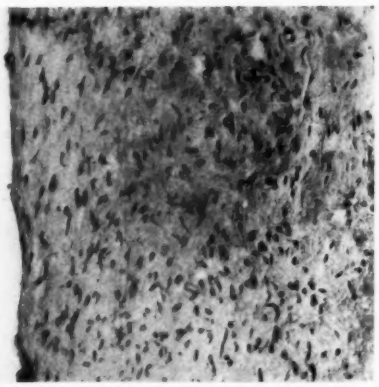


Fig. 5. Case 3. Photomicrograph of hygroma. The cyst wall is comprised of rather dense connective tissue of low vascularity. The lining membrane consists of a thin endothelium. ×170.

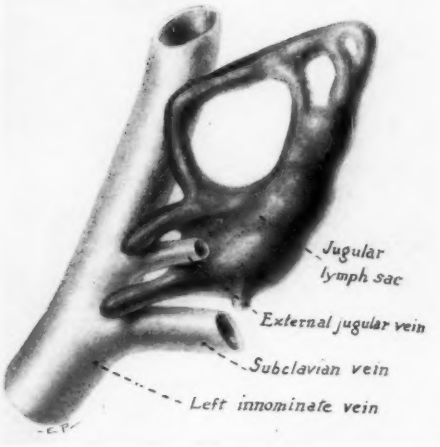


Fig. 6. Reconstruction of a left jugular lymph sac from an 11 millimeter cat embryo, showing relation of the lymphatic anlage to the cervical veins (after McClure and Silvester).

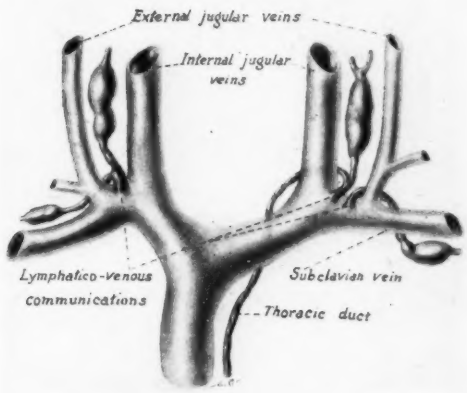


Fig. 7. Sketch showing position of the lymphatic buds of the neck and their communications with the venous system as found in the embryo of a monkey (Macacus nomestrinus Linn) (after McClure and Silvester).

small. The cyst fluid is characteristically thin, clear, and usually colorless though it may possess a very slight yellowish tinge.

Microscopic findings. The fibrous wall is composed of connective tissue of variable cellurity (Fig. 5). Collagen may be abundant and compact, or may be scanty and have a myxomatous appearance. Even in the absence of infection there are isolated lymphocytic cell infiltrations, and it is not uncommon to encounter lymphoid follicles with germinal centers. Blood vessels are mostly of capillary and arteriolar size, larger channels seldom being seen. A thin layer of flattened endothelial cells lines the cystic spaces (Fig. 9). Occasionally a blood vessel, nerve, or small muscle bundle traverses a crypt or outpocketing of the main cyst cavity, and in each instance this traversing structure is surrounded by a single layer of endothelial cells.

Goetsch has added greatly to our understanding of the pathological processes in this lesion, particularly in reference to its manner of growth and propagation. According to his conception there are narrow outgrowths of cords of endothelial cells which grow between muscle bundles, nerve fibers, and other structures of the neck. While these cords are at first solid, they later acquire a lumen by the accumulation of a lymph-like fluid which forces apart the walls to form an endothelial lined sac, which either abuts against the main cyst cavity or else attains a communication with it. The continued collection of fluid in one of these side pockets or daughter cysts enlarges this wedge between the anatomical structures of the neck, so that eventually a muscle fiber, a blood vessel, or nerve becomes separated from its supporting structures and is surrounded by a layer of endothelial cells. In this way a small strand of muscle, an artery, etc., appears to finally *traverse* the cavity of a hygroma and may be atrophied by pressure from the surrounding fluid.

SYMPTOMS

As might be expected, a cystic hygroma usually gives little in the way of troublesome symptoms. Pain or local discomfort is rarely encountered unless secondary infection has occurred. The tendency of such a cyst to lie in a superficial plane of the neck permits it to bulge outward and thus be directed away from the important and deeply lying cervical structures. Hence it is rare to have interference with the normal functions of the brachial plexus, the great vessels, the esophagus, or the trachea. While the softness of the

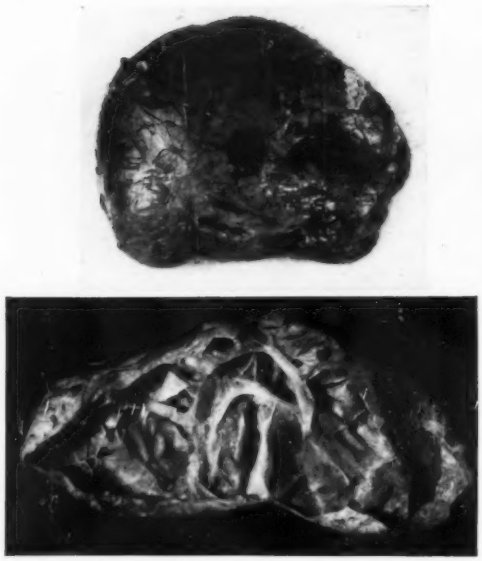


Fig. 8. Case 5. Photographs of surgically excised cystic hygroma. Cyst measured 5 by 4 by 4 centimeters. Lower picture shows the thin walls which are characteristic of the sac and also the trabeculæ which are often found coursing through the cavity.

Fig. 9. Case 5. Photomicrograph of cyst wall showing the endothelial lining. ×1025.

tumor and its tendency to outward displacement usually protect the deep structures from damage, 2 of our patients had definite tracheal compression and another had interference with mastication by protrusion of the cyst into the floor of the mouth. Goetsch reports a patient who had respiratory embarrassment due to low tracheal obstruction by a prolongation of the mass well down into the mediastinum. The larger hygromas may be bothersome because they limit the free movements of the head and neck merely by their great size. In short, then, such a patient—or his parent—complains primarily because of the presence of a lump or the disfigurement which is associated with it.

The local mass is observed for a variable length of time before medical attention is sought. Some patients are directly referred by the obstetrician who has noticed the lesion at birth. It is not uncommon, however, that advice is not sought for many months or even several years, because the rather innocuous appearance of the smaller lesions may excite little curiosity or anxiety. It is characteristic of some hygromas to lie rather dormant or to increase in size only slowly over a long period of time and then to have a sudden augmentation in size which brings the patient to the physician's care.

In 3 patients we have noted a relationship between the presence of an upper respiratory infection and the subsequent sudden enlargement of a previously existing cystic hygroma. Apparently the infection has led to plugging or partial obstruction of the normal lymphatic channels so that there is a backing up of lymph in the hygroma which causes it to enlarge. While we have no microscopic proof that there are communications between a hygroma and the normal lymphatic spaces of the neck, these isolated observations make us feel that such anastomoses do actually exist.

In 2 of the patients (Cases 11 and 21) noted in the preceding paragraph there was suppuration within the hygroma. In Case 21, a boy 3 years of age, the cyst had been noted since birth but little attention had been paid to the mass until it had become infected. The local findings of course then changed to present all of the cardinal signs of inflammation, combined with a severe systemic reaction and a pneumococcus bacteremia from which he eventually recovered. This case, along with 2 others showing wound sepsis following partial excision of cysts, have demonstrated that suppuration in these lesions is an extremely

a b c d

Fig. 10. Case 11. a, Eleven months old boy with small, recurrent hygroma on right side of neck. b, Scar shows site of previous operation, at which time an incomplete removal had been performed. c and d, Photographs 4 years after partial excision, radium therapy, suppuration, and incision and drainage.

dangerous complication, not only because of the rapidity with which it spreads through the local regions of the neck but also because of the great probability of bacterial invasion of the blood stream.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Recognition of a hygroma rarely offers any real difficulty. Certainly, in those children in whom there is a large, lobulated, bluish mass which is covered by a very thin skin and which can be transilluminated, there should be no question in making a correct diagnosis. If the swelling arises in the supraclavicular fossa or elsewhere in the posterior cervical triangle, most of the other confusing lesions of the neck, including thyroglossal duct cyst and branchiogenic cyst, can be ruled out at once. However, when a small hygroma which is unilocular and smoothly rounded is found in front of the sternomastoid muscle these 2 other lesions may be differentiated only with difficulty. Points in favor of a hygroma are its ability to transmit light, the rather ill defined borders of the mass, and the soft and flabby consistency. Opposed to these findings, the cysts arising from the branchial system or thyroglossal duct are not as large, are more tensely filled, are apt to have a thicker wall, a better defined border, and transmit light only rarely. The branchiogenic cyst may be found anywhere along the anterior border of the sternomastoid muscle, particularly in its lower one-third; but attempts to move the cyst usually disclose some attachments to deep cervical structures (14) which are not such a prominent feature in the hygroma. The midline position of a thyroglossal duct cyst sets it apart from a hygroma, which, if it occurs in the midline, always has extensions well out to one side of the neck.

Dermoid cyst of the neck may occasionally be considered in the differential diagnosis. It usually can be excluded because of the superficial position of the lesion, its attachment to the skin, and the doughy and plastic consistency of the mass. Malignant neoplasms are at times subject to cystic degeneration, but there is always some remaining solid and palpable tissue which indicates the true nature of the swelling. A deeply seated hemangioma

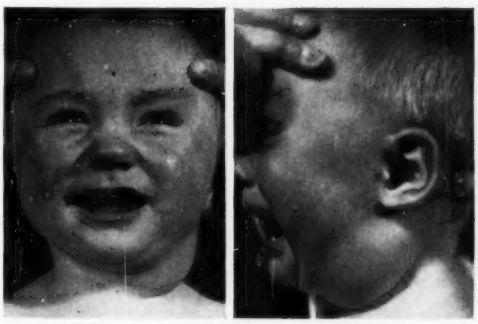
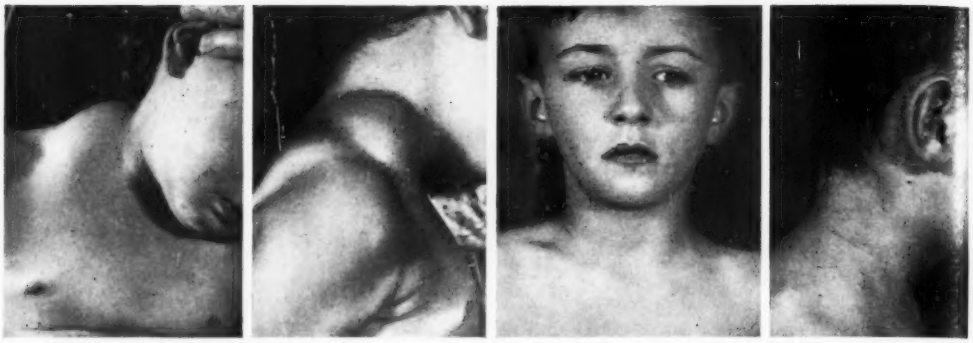


Fig. 11. Case 15. Eighteen months old girl with a left cystic hygroma which had been noticed for 9 months.



a b c d

Fig. 12. Case 16. a and b, Pre-operative photographs of a 20 months old male child with cystic hygroma high on right shoulder. c and d, Postoperative photographs taken 6 years after surgical excision of hygroma.

is usually compressible and while the smaller specimens may give no discoloration of the overlying skin, certainly the larger vascular tumors will possess a reddish or bluish color on their external surface. An infected hygroma may be confused with tuberculous adenitis or cervical abscess, but the history of a known swelling for a long period of time prior to onset of the infectious process should lead one to suspect that suppuration has secondarily occurred in a congenital hygroma.

ETIOLOGY

In studying the etiology of cystic hygromas it is a temptation to group them with the lymphangiomas found in the neck and in other regions of the body. Lymphangiomas are more often encountered in skin and subcutaneous fat or superficial tissues, particularly in the lip, axilla, anterior chest wall, arms, or legs. There would be little objection to the classification of hygromas with such lesions, regarding these as cystic or cavernous lymphangiomas. Indeed, some authors have freely used the terms hygroma and cavernous lymphangioma as being synonymous and can offer histological material to support this view. However, there are 2 principal reasons for objecting to this grouping together of the 2 conditions. First, lymphangiomas of the lip, hands, feet, etc., rarely develop cystic cavities more than a few millimeters in diameter. Thus, from these observations in other parts of the body it is probably within reason to assume that lymphangiomas do not form such large cysts as are found in hygromas of the neck. Second, the rather sharply defined areas in which hygromas are found in cervicoaxillary tissues and, less commonly, in the groin or retroperitoneal spaces, lead one to connect their origin with 2 known embryological structures which are present in these 2 regions, namely, the *lymphatic sacs* of the neck and the *iliac areas*.

According to Sabin there arises from the jugular vein a small, endothelial lined outpocketing which subsequently becomes detached from the vein and develops as the primitive *lymphatic sac or bud*. This structure is paired and is found on either side of the neck (Figs. 6 and 7). At about the same stage of fetal life there are other smaller structures of a similar nature which arise in relation to the large pelvic veins. Less important centers for the development of these lymphatic anlagen are found along the dorsal aspects of the abdomen and thorax. Arising from these various buds, particularly from the large cervical ones, the growing lymphatic vessels coalesce and become a unified anastomosing system which later acquires permanent communications with the venous channels.

This preceding view is challenged by Huntington and others who believe that the endothelium lined lymph sacs of the neck and other portions of the body trunk do not arise as offshoots of the venous system, but rather that they develop directly from mesenchymal

a b c d

Fig. 13. Case 20. a and b, Pre-operative photographs of 2½ year old boy with hygroma of left side of face and neck. Two x-ray treatments (250 roentgens each) did not reduce size of the mass. c and d, Postoperative photographs taken 9 days after complete excision of the hygroma. In d, the cervical skin is still pigmented from x-ray irradiation and is also still redundant following the operation. (Pigmentation and wrinkles subsequently disappeared.)

tissues and then, after a period of ramification and coalescence, they acquire a communication with the venous channels.

Whichever of these 2 views is correct is not pertinent to the present discussion. Suffice it to say that there is agreement among embryologists concerning the presence of the jugular and other lymphatic sacs in the human and other vertebrate fetuses. The positions of these structures and the similar anatomical positions of hygromas appear to leave little doubt (McClure, Thompson and Keiler) that a pinching off or sequestration of tissue from one of these embryological lymphoblastic islands or channels gives rise to an endothelium lined lesion which we know as the hygroma.

TREATMENT

In the treatment of cystic hygromas several forms of therapy are available. In order to present the factors in favor of or against a given method, it is advisable to consider the various therapeutic procedures individually.

1. Expectant treatment. Some authors, notably Fraser, have advised that surgical attempts aimed at removal should be withheld for an indefinite length of time because of the tendency of a hygroma to undergo spontaneous regression. This teaching cannot be

Fig. 14. Case 20. Roentgenogram of cervical hygroma showing shadow of uniform density lateral to the jaw and face. Compare with Figure 13.

Fig. 15. Case 20. Photograph of cut surface of surgica specimen (12 centimeters long and 9 centimeters wide). Multilocular development. Extensive thickening and fibrosis of external wall and intervening septa presumably due to previous x-ray irradiation.

a b c d

Fig. 16. Case 21. a and b, Photographs of 3 year old boy with a hygroma which had been present since birth. (This cyst subsequently became infected following an upper respiratory infection. Incision and drainage of the suppurating cyst led to complete disappearance of the lesion.) c and d, Photographs taken 5 years later. No recurrence of hygroma following its suppuration and incision and drainage.

a b c d

Fig. 17. Case 22. a and b, Pre-operative photographs of 3 year old girl with a hygroma which had been present for 2 years. c and d, Postoperative photographs which were taken 5 years after the surgical excision of hygroma, showing normal contour of the neck and an almost invisible cutaneous scar.

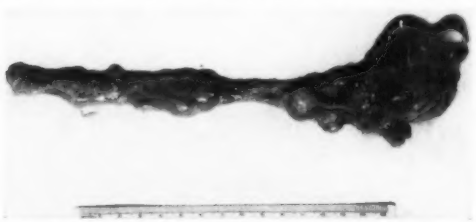


Fig. 18. Case 27. Photograph of surgically removed hygroma. There are multiple, contiguous, thin-walled cysts. The enlarged portion of the specimen at the right presented in the neck, and the slender part toward the left extended along the brachial plexus into the axilla. (Case of Dr. John Homans from the Peter Bent Brigham Hospital.)

supported by our observations, for in children who have been followed for several years we have yet to see a patient in whom there has been a spontaneous disappearance of the mass. It is true that the cyst, or cysts, may decrease in size from time to time, but they will again refill, and, in general, we have found that there is always a progression in size if the patient is followed over a long period of time. Hence, our experience does not permit us to endorse the idea of "expectant treatment," and indeed there is much to be said against it for the tendency of a hygroma to suppurate after respiratory infections makes it desirable that this serious complication be avoided by early excision of the cystic mass.

2. Spontaneous regression following infection. The introduction of an infectious agent into a

hygroma, of course, cannot be employed as a therapeutic procedure because of the lack of measures to control it. However, if suppuration does occur in a hygroma and the patient does not die of generalized sepsis, there is a strong likelihood that the hygroma will be cured because of destruction of the lining membrane by the inflammatory process. We have seen 2 examples of this in which, following tonsillitis and an upper respiratory infection, the purulent exudate accumulating in previously existing hygromas necessitated incision and drainage. Subsequent to the disappearance of the sepsis and the healing of the wound there has been no recurrence of these 2 cystic lesions in a period of 5 years during which they have been followed.

3. Aspiration treatment. As early as 1839, Arnott advocated the use of aspiration in small infants with large cysts who might not be able to stand the insults of a surgical procedure. In a 1 month old baby he performed repeated aspirations until the child was 4 months of age and surgical excision was possible. In only 1 instance have we attempted this and, after multiple needlings, the stagnant fluid within the cyst became infected. We have, therefore, discouraged the use of the procedure and would advise it only as an emergency measure for relief of pressure symptoms such as might occur with displacement of the larynx or with compression of the great neck vessels.

4. Injection of sclerosing agents. This has been suggested by MacGuire and others. Harrower has advocated the use of sodium morrhuate because he felt that open operation carried too high a mortality rate. In his patient 2 cubic centimeters of 5 per cent sodium morrhuate were injected into the swelling. On the following day the mass had increased to one and a half times its previous size, but on the third day it began to shrink. Six days later a second such treatment was given and, though there was some postoperative local reaction, the mass had entirely disappeared in a month. After a study of pathological material, it would seem that the thinness of the lining of a hygroma would make the lesion almost ideal for injection therapy, because the sclerosing agent could be easily diffused through the fluid medium and would not have to penetrate deeply into the tissues to destroy the endothelial layer. However, a word of caution must be inserted regarding this method of therapy. The hygroma is apt to dissect downward to the large vessels of the neck and partially or completely surround them. If, under such conditions, a necrotizing agent is introduced into the hygroma sac, it is possible that damage or thrombosis of the internal jugular vein or carotid artery could ensue. Furthermore, the introduction of a sclerosing fluid into the sac may be disastrous in certain cases in which there appears to be a definite communication between the hygroma and the venous system. What appeared to be such a connection was well demonstrated in Vaughn's patient who was studied roentgenographically after the introduction of iodized oil into the hygroma. X-ray plates taken immediately after the injection showed clearly the outlines and extent of the cystic swelling, but a plate one-half hour later showed complete disappearance of the opaque medium which presumably had run off into some communicating vein. It is not difficult to contemplate the possible complications had a sclerosing solution been introduced into this lesion. Therefore, the likelihood of overlooking a small lymphaticovenous anastomosis leads us to discourage the injection therapy in all cases.

5. Use of setons. The use of a seton to attempt destruction of a hygroma has been advocated by several authors. Volker performed this procedure on a newborn child who died 16 days later. Smith reported 5 hygromas, 4 of the neck and 1 of the chest, treated with setons consisting of a single thread of fine silk which was led through less prominent portions of the tumor, allowing some inflammation and induration to occur before withdrawing the thread. However, we agree with Gurlt that the procedure is dangerous on the grounds that diffuse uncontrollable suppuration and fatal infections are apt to occur.

6. Radium or roentgen ray irradiation. New, in 1924, was the first to treat a hygroma successfully with radium. Figi has been the principal proponent of radium therapy. He treated a series of 12 cases from the Mayo

Clinic, employing from 3,000 to 7,000 milligram hours of radium (applications made at a distance of 2.5 centimeters, using 2 millimeter lead screening). These were repeated at intervals of 2 or 3 months, the average patient receiving 4 treatments. Seven of these cases died of sepsis originating in the local lesion, but 4 had been infected prior to the first application of radium. Of the 5 patients who survived, 3 were entirely cured and the 2 remaining were much improved.

Radium has been employed in only 1 of our patients (Case 11). Following surgical excision there was a recurrence for which radium therapy was begun on the twenty-second postoperative day, 65 milligrams of radium being used for 4 hours to each of 4 separate areas. Within 2 months there was complete disappearance of the mass, but 2 years later there was a recurrence. The recurrent cyst became infected, was incised and drained, and has not reappeared in the subsequent 5 years during which it has been followed.

X-ray irradiation was employed in Case 20 of our series (Fig. 13). Without previous therapy the treatment was given with diffuse exposure over the cyst employing 160 kilovolts, 5 milliamperes, tube distance of 40 centimeters, for 26 minutes, with filters of ¼ millimeter copper and 1 millimeter of aluminum. This dose of approximately 250 r units was repeated 1 month later. For the ensuing 2 months under observation there was no appreciable reduction in size of the mass, and surgical excision was subsequently resorted to with success.

In general, then, it may be stated that radium or x-ray irradiation is not a very promising therapeutic measure and should be employed only for those cases in which there is mediastinal involvement or in which there is some other disease which contra-indicates operative excision.

7. *Surgical excision.* The complete removal of a hygroma by surgical dissection has proved to be the most satisfactory method of treatment. Many surgeons have evaded this undertaking believing that the young patient does not take an anesthetic well, that the dissection is tedious and difficult, and that the attendant mortality is high. Contrary to these statements, it has been our experience that a child, even a newly born infant, will tolerate ether anesthesia extremely well if administered by a capable anesthetist, that the excision of a hygroma can be performed with thoroughness if care is exercised, that the resulting mortality is low, and that permanent cure can be expected.

In all cases we have employed ether, or avertin (80 milligrams per kilogram) with ether, and have found these extremely satisfactory. Great muscular relaxation is not required and the necessary depth of anesthesia can be maintained over a long period of time without difficulty.

In general, the skin incision should be made in a direction which will later correspond to the normal folds of the neck. If the mass is relatively small, none of the overlying skin need be cut away; but if the hygroma is large, it may be desirable to remove an elliptical portion of the skin so that there will not be too much excess tissue when the cutaneous flaps are later brought together. It is not necessary, however, to plan on an accurate adjustment of the skin folds to remove wrinkles at the time of the wound closure, for it has been amply demonstrated that large and disfiguring cutaneous folds will disappear rapidly and a pleasing contour of the neck will be re-established in a few months time (Fig. 3).

The dissection and removal of a hygroma is usually easy if patience is exercised and haste is avoided. The overlying skin, though tense and thin, will readily separate from the underlying cyst. If the wall of the cyst is closely followed, blunt dissection will disclose a plane of cleavage leading almost entirely around the mass. When the proper plane of cleavage is found and followed, little bleeding is encountered for vessels running to the hygroma are quite small in size and few in number. In general, the large unilocular cyst is more easy to dissect than is the small, multilocular lesion which is apt to be very adherent to surrounding structures.

The cyst wall is little more than tissue paper in thickness and tends to tear easily, hence it is important not to grasp the cyst with instruments but rather to hold it with the gloved hand or with a piece of moist gauze.

Every effort should be made to keep the cyst intact, for as long as this is done the borders of the structure are readily definable; but once the mass has collapsed there may be prolongations outward between the muscles or vessels of the neck which will be cut across and be overlooked. Such an island of tissue which is left behind must necessarily act as a focus for recurrence of the lesion. Hence, meticulous technique must be employed to prevent rupture of the cyst and to avoid leaving bits of the endothelial lining if subsequent recurrence is to be avoided.

The removal of a hygroma may lead the operator extensively into the planes of the neck for it is the nature of the lesion to possess projections along the great vessels, between muscle bellies, along the brachial plexus, into the axilla, or downward over the surface of the apical pleura. Such a behavior at once implies that care must be employed in order to insure that all of the contiguous and important structures of the neck might be left uninjured. The internal jugular vein, carotid arteries, and branches of the brachial plexus are all large enough so that they can be easily identified and avoided, but the hypoglossal nerve and the lower filaments of the facial nerve are apt to be overlooked and severed with resulting distressing deformity. Mason and Baker have recommended that for tumors high in the parotid region it is safer to incise the skin well up behind the ear and first expose the facial nerve so that it can be identified along its entire course as the subsequent dissection proceeds anteriorly. In affirming this teaching, we would also add that whenever the dissection carries one in front of the sternomastoid muscle it is best to identify the spinal accessory nerve immediately so that it can be isolated and retracted to the upper border of the operative field.

The wound should be closed so that the edges of the platysma muscle are approximated. If this is done painstakingly, there will be little tendency for separation of the skin margins and the resulting cutaneous scar will be minimal and almost invisible (Figs. 12 and 17). Drainage of the wound is not necessary if hemostasis has been complete. The dressing must be carefully applied to insure against accumulation of plasma and to promote adequate anchoring and healing of the undermined flaps of skin.

In nearly all cases the hygroma can be removed completely at a single operation. However, in an infant a few weeks of age with a very extensive growth, in whom operation is imperative because of respiratory distress, it would probably be best to plan a multiple stage procedure, removing only a portion of the growth at each stage.

The operative mortality should be low. In 25 of our patients surgical removal of the cyst was performed in 1 or more stages with 2 deaths. In one of these cases there was sepsis in the cyst prior to operation and probably excision should not have been undertaken. In the other fatal case suppuration occurred in the wound subsequent to the operation and the patient died of diffuse cellulitis of the neck and a resulting bacteremia. Recurrence of a hygroma should be rare if surgical excision is properly performed. In 3 of our patients only a portion of the hygroma was removed at the first stage, leaving the complete excision of the remaining cyst wall until a latter sitting. In every case following such multiple stage procedures all of the cyst could be finally removed and there was no recurrence. Likewise, in all cases in which the hygroma was completely excised in 1 operation, no patient had a recurrence.

SUMMARY

1. Experiences with 27 cases of hygromatous cervical cysts are reported. Cystic hygroma of the neck is a lesion occurring chiefly in infancy and childhood. It is first noticed in about half the cases at birth and is observable in 90 per cent of the patients by the end of the second year, yet the first onset of the swelling may not appear until later childhood or even adult life. The mass grows slowly and is composed of a thin walled cyst (or cysts) which is lined by an endothelial layer of cells and which is filled by a clear and colorless fluid. The specimen may vary in size from a few centimeters in diameter to one which may be larger than the patient's head.

2. The lesion is a congenital one and is presumably derived from rests of endothelial cells

which were split off and isolated from the fetal lymphatic system which arises from the primitive *lymphatic buds* of the neck.

3. The enlarging cyst may give symptoms from pressure on the trachea, pharynx, or other structure of the neck. It may be so large as to interfere with movements of the head and neck. In the average case there are no distressing symptoms but there is marked cosmetic disfigurement. There is a distinct tendency for a hygroma to suppurate, particularly following an attack of tonsillitis or an upper respiratory infection. If bacterial invasion of a hygroma does occur, there are profound constitutional symptoms; for bacteremia may follow and the resulting mortality is very high. Therefore, all hygromas should be removed in order to avoid the dangers of infection and its complications.

4. Treatment with the use of sclerosing fluids is probably hazardous because of the possibility of introducing some of the necrotizing agent into the general lymphatic or venous systems by way of small unsuspected communications. The use of radium or roentgen ray irradiation as a therapeutic measure has given irregular and disappointing results.

5. The treatment of choice is complete surgical excision. This can be accomplished usually in one stage except in those instances when the cyst is extremely large. The mortality from operative treatment should be very low and the incidence of recurrence should be negligible.

6. In the present series of 27 cases there were 2 deaths following operation, both attributable to sepsis. In 1 of these the cyst was infected prior to operation; in the other the wound was infected subsequent to the surgical procedure. In the 22 patients who have been followed from 1 to 13 years after operation there has been no recurrence of the hygroma in any case. The cosmetic results following excision of the cysts have been excellent.

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THE USE OF PROSTIGMIN METHYLSULFATE IN THE PREVENTION OF POSTOPERATIVE INTESTINAL ATONY AND URINARY BLADDER RETENTION

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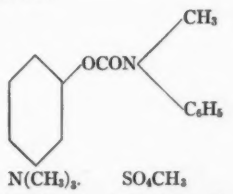
THE possibility of postoperative intestinal atony and urinary bladder retention must be considered in all major operations, particularly in those below the diaphragm. According to Jordan, some degree of urinary retention occurs in 50 to 80 per cent of patients after operation; similarly postoperative intestinal atony, as reported in the literature, also frequently occurs. Surgeons therefore welcome a method which successfully reduces or prevents the incidence of these complications. The importance of prostigmin[1] in the *treatment* of paralytic ileus is well-established; in this report we are concerned only with the use of prostigmin as a preventive against postoperative intestinal distention and urinary retention. It is our belief that prostigmin is of definite value in preventing the postoperative occurrence of these two conditions.

For years it has been known that physostigmine aids in overcoming intestinal distention, but the undesirable by-effects of this drug prevent its routine use.

In 1931 White and Stedman determined that the physiological properties of physostigmine were dependent on the presence of the urethane group in the molecule, and they were able to demonstrate that alkyl substituted phenyl esters of carbamic acid in a manner similar to physostigmine. Following this lead, Aeschlimann and Reinert experimented with these esters and concluded that the dimethyl and the methylphenyl carbamic esters of 3-hydroxyphenyl trimethyl ammonium methylsulfate were at least equally as effective in their action on the intestine as physostigmine.

The methylsulfate salt of the dimethyl ester was finally chosen as the most desirable compound and was made available for clinical use under the trade name of prostigmin.

The drug is non-hygroscopic and is stable in aqueous solution. The molecular structure is less complicated than that of physostigmine, and is as follows:



Dimethyl carbamic ester of 3-hydroxyphenyl trimethyl ammonium methylsulfate.

The ampul solutions of the drug are suitable for subcutaneous or intramuscular injection.

The activity of the body cells under the control of the autonomic nervous system is determined by the balance struck between the stimulation of the sympathetic and parasympathetic divisions of the system. The stimulation or drive of the parasympathetic nerves is effected or attended by the release of acetylcholine at the junction between the nerve termination and the receptor tissue, which acts as a bridge for the free flow of energy from effector to receptor tissue, resulting in cellular action. Choline esterase, also present at the junction, eventually destroys the acetylcholine after a physiological interval, and thus terminates the stimulation of the parasympathetic nerve endings. On the basis of these concepts, alteration of the acetyl-

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[1]There are two salts of prostigmin—prostigmin methylsulfate and prostigmin bromide. Prostigmin methylsulfate is available in 1 cubic centimeter ampuls of 1:2000 solution and 1:4000 solution. To avoid burdensome detail, hereafter in this report ampuls of the 1:2000 solution will be referred to as prostigmin regular, and ampuls of the 1:4000 solution as prostigmin prophylactic. Prostigmin bromide is available as oral tablets and is used in the treatment of myasthenia gravis.

choline-choline esterase balance, or the use of drugs affecting their interaction, stimulates or depresses parasympathetic activity. Prostigmin inhibits choline esterase and therefore is a cholinergic drug. In the postoperative patient, there is apparently an autonomic imbalance, with either sympathetic stimulation or parasympathetic paralysis. This hypothesis affords a physiological explanation of the relaxation of the intestinal and bladder musculature, manifested clinically as intestinal atony and urinary retention. Prostigmin, being a cholinergic drug, arouses parasympathetic activity which is followed by increased tone and peristaltic activity of the intestinal and vesical musculature.

This effect of prostigmin on intestinal tonus has been demonstrated experimentally (22). The action on the bladder is less evident. Myerson has shown that the administration of prostigmin combined with acetyl-beta-methylcholine is followed by very marked stimulation of the bladder musculature; however, the use of the combination appears to have dangers which outweigh the clinical advantages, in light of present knowledge.

Prostigmin, in the therapeutic dosages ordinarily employed in postoperative atony and retention (i.e., 0.25 to 1.0 mgm.) is free from undesirable by-effects on the cardiovascular system, the pupil, the sweat-glands, and the salivary glands (6). Toxic symptoms in the normal human being after the oral ingestion of 90 milligrams of prostigmin have been described by Goodman and Bruckner as follows: bradycardia, intestinal discomfort and activity, shock, skeletal muscle activity, spasm of accommodation, and miosis. Atropine was found to be a specific antagonist.

Prostigmin, in the prevention and treatment of intestinal atony, has been the subject of numerous reports in the literature. One of the most recent reports comes from Harger and Wilkey who employed prostigmin with complete satisfaction in 175 postoperative abdominal cases. These authors used the 1:4000 solution at 2 hour intervals with no untoward after-effects.

There are relatively fewer articles on the use of prostigmin in postoperative urinary bladder retention. Duschl was one of the first to be impressed with its value in this condition. Several other investigators have found prostigmin an aid to micturition in the post-surgical patient.

We used prostigmin in a series of 253 operative cases, of which 250 were studied for intestinal distention and 247 for urinary bladder retention. Three of the cases involved such surgical procedures as first stage colostomy and could not be studied from the standpoint of intestinal atony, and 6 involved operations on or near the bladder where catheterization was routine.

The intestinal group was divided into those cases in which there was no distention detectable, those with slight and brief periods of distention, those with moderate distention lasting up to 36 hours, and those with severe distention lasting more than 36 hours.

The diagnosis of urinary retention was based on the necessity for catheterization, which was done at the eighteenth hour after operation, or before that time if the patient complained of discomfort.

The intestinal distention series and the urinary retention series were each subdivided into three groups: (A) those receiving prostigmin both before and after operation, (B) those receiving prostigmin before operation only, and (C) those receiving prostigmin after operation only.

In groups A and B, when possible, three injections of prostigmin were given at convenient intervals over the period of 18 hours immediately preceding operation. In groups A and C the administration of prostigmin was started within 4 hours of the patient's return from surgery and continued at 4 or 6 hour intervals for a total of 4 to 6 doses, or more if distention or retention appeared imminent. A soft rubber tube was inserted into the rectum routinely for a period of one-half to one hour after each injection of prostigmin. The results are given in Tables I and II.

We began our investigation using the 1:2000 solution of prostigmin (prostigmin regular) in 1 cubic centimeter doses. Later, a supply of 1:4000 solution (prostigmin prophylactic) became available. We continued the trials using the latter strength without, however, increasing the number of doses or de-

TABLE I.—POSTOPERATIVE URINARY RETENTION—247 CASES

	Prostigmin given		After operation only
	Both before and after operation	Before operation only	
No catheterization	87	13	134
Catheterized once	2	0	2
Catheterized more than once	1	0	8
Percentage catheterized	3.3	0	6.9

TABLE II.—POSTOPERATIVE INTESTINAL ATONY—250 CASES

	Prostigmin given		After operation only
	Both before and after operation	Before operation only	
No distention	85	13	125
Slight distention	2	0	11
Moderate distention	3	0	7
Severe distention	1	0	3
Percentage with distention	6.6	0	16.8

TABLE III.—RESULTS ACCORDING TO STRENGTH OF PROSTIGMIN SOLUTION

	Total cases	Distention	
		Cases	Per cent
Prophylactic (1:4000) only	99	11	11.1
Therapeutic (1:2000) only	140	15	10.7
Both prophylactic and therapeutic	11	1	9.1
	250	27	
	Total cases	Catheterized	
		Cases	Per cent
Prophylactic (1:4000) only	98	5	5.1
Therapeutic (1:2000) only	138	7	5.1
Both prophylactic and therapeutic	11	1	9.1
	247	13	

creasing the interval between injections. Prostigmin prophylactic (1:4000) was equally as effective as prostigmin regular (1:2000) in preventing distention and retention of urine (Table III).

In groups A and B combined, in which prostigmin was given before operation, the incidence of intestinal distention was reduced to 5.7 per cent. In group C in which prostigmin was given only after operation, the incidence of distention was 14.4 per cent. No ill-effects resulted from the continued use of prostigmin after end-to-end anastomoses and other types of gastro-intestinal surgery. It was interesting to note at the operating table how much better the tone of the bowel was in those patients who had received prostigmin before operation.

In the urinary retention series, those patients receiving prostigmin before operation required catheterization in but 3.9 per cent of cases, while 6.9 per cent of those receiving the drug only after the operation had to be catheterized. It was observed during the earlier months of study that some patients, during the twelfth and eighteenth postoperative hours, experienced a desire to void but were unable to do so until toward the end of that period. To aid these patients one of us (E. G. W.) devised the plan of giving each patient, in addition to the regular routine doses, a 1 cubic centimeter injection of 1:2000 prostigmin every hour for a total of three injections. This resulted in the most gratifying response. Most of the patients voided after the first or second injection and in no case was catheterization necessary.

No patient in the combined series exhibited any marked lowering of the blood pressure or slowing of the pulse. There was no appreciable degree of miosis, impairment of accommodation, or sweating. This is in agreement with the findings of other investigators. One patient, 4 months pregnant, received the routine prostigmin dosage without any disturbance of the gravid state. Some patients received as many as twenty-four 1 cubic centimeter doses of 1:2000 prostigmin. Subjective complaints were rare, and "gas pains" were very infrequent. Only one patient, a graduate nurse, experienced abdominal discomfort directly referable to the drug itself. This girl complained of mild upper abdominal pain lasting for a few minutes after each injection had been given. The pain ceased as soon as the administration of prostigmin was concluded.

CONCLUSIONS

Prostigmin given prophylactically both before and after operation is effective in reducing the incidence of postoperative intestinal atony and urinary bladder retention.

The prophylactic (1:4000) strength of prostigmin appears to be as effective as the therapeutic (1:2000) strength in preventing postoperative distention and retention of urine.

If the usual prophylactic routine seems insufficient to control urinary retention, the hourly administration of 1 ampul of 1:2000 prostigmin for three consecutive injections gives the desired result.

In the series reported, we found no contraindications to the use of prostigmin, and we observed no untoward results. A case in which there was mild abdominal discomfort following the administration of prostigmin is described.

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ECTOPIC PREGNANCY

A Review of Three Hundred Ten Operative Cases

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THIS is a study of 310 cases in which patients were operated upon for ectopic pregnancy, or operated upon for some other condition but with an ectopic pregnancy found at operation, during a 7 year period from 1930 to 1936 inclusive from the gynecological service at Bellevue Hospital. All of these patients presented a history and symptoms warranting admission to the hospital, even though immediate operation was not always performed; and varying periods of observation were frequently necessary before a diagnosis was established. In spite of careful observation, sometimes rather prolonged, the diagnosis was often incorrect as will be shown.

ANALYSES OF DATA

Of the 310 cases, 9 were under 20 years of age. Eight-two were from 20 to 25 years, 96 from 25 to 30 years, 79 from 30 to 35 years, 35 from 35 to 40 years, and 9 were over 40 years of age. It is obvious that the majority of cases occurred between the ages of 20 and 35 years (257). The incidence under 20 and over 40 years was comparatively low.

There were 36 colored patients, 273 white and 1 yellow. It is interesting to note, and perhaps of some significance, that the incidence of ectopic pregnancy in the colored race is approximately 11 per cent, although the total admission to the gynecological service runs close to 40 per cent with an extremely high incidence of salpingitis. An explanation of this observation is a matter for speculation.

The most common infections and in order of frequency were: measles, 127; whooping cough, 56; mumps, 42; and pneumonia, 24. There were 115 patients who had had no previous operations, 50 who had had 1 or more curettages, 46 who had had appendectomies, 37 who had had previous abdominal gynecological operations, and only 9 who gave a definite history of previous ectopic pregnancy. From these figures we can conclude that there is an unusually high incidence of previous lower abdominal surgery, not including previous ectopics. A definite history of pelvic infection was obtained in 59 cases, 42 of which were gonorrheal, 10 postpartum, and 7 postabortal. It is very likely that lesser grades of pelvic infection, either gonorrheal or otherwise, were never severe enough to be considered by the patient and therefore not obtained in the history. In spite of this, there is still an incidence of less than 20 per cent of pelvic infection.

In 99 instances, the interval since marriage was not stated, 20 patients were not married, and in 10 the interval was less than 1 year. It is interesting to note that 66 had an interval of more than 10 years, and 58 more than 5 years since marriage, a total of 124 out of 211 who were married 5 or more years.

The opinion is prevalent that a period of complete or relative sterility exists prior to the occurrence of an ectopic pregnancy. It is difficult to evaluate correctly all our figures, because of the 77 who were not previously pregnant, we are unable to say how many practiced contraception or were unmarried. More than one-third (119) occurred in less than 5 years following a previous pregnancy. In more than one-sixth (53), 5 years or more elapsed since the last pregnancy. In about 10 per cent (27), the interval was less than 1 year. From our observations it would seem that overemphasis has been placed on the sterility period prior to the occurrence of an ectopic pregnancy. Practically an equal number of patients showed an incidence of less

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than 2 pregnancies (154) as showed more than 2 pregnancies (153). The number of previous pregnancies appears to bear no relation to the incidence of ectopic pregnancy. In our 240 ectopic pregnancies, 128 patients gave a history of 1 or more abortions, spontaneous, induced or both. There were 86 spontaneous and 36 induced abortions. While the number of spontaneous abortions outnumber the induced abortions by 50, we are not convinced that either play a rôle in the causation of ectopic pregnancy. The same, we feel, is true as regards term pregnancies.

The greatest number of patients complained of a colicky pain, severe in degree, and irregular in continuity. In the next larger group, the pain was lancinating in character, moderate in severity, and constant. As regards radiation of pain, it is interesting to note that in approximately two-thirds of the patients (193), the pain was generalized over the entire abdomen, next in frequency being the right or left lower quadrant, with comparatively few radiations to one or both shoulders. The following shows the exact figures:

The type of abdominal pain was colicky in 170 patients, lancinating in 107, aching in 51, no abdominal pain present in 4, and no report was given for 5. The pain in 226 patients was severe, in 76 moderate, in 31 only slight, and in 8 patients the degree of abdominal pain was not reported. Two hundred nineteen patients reported that the pain was irregular, 70 that it was constant, 9 that it was rhythmic, and 16 did not state anything relative to the continuity of pain. Pain radiated to one or both arms in 26 patients; one or both shoulders in 65; to the left or right abdominal quadrant in 79; epigastrium, 26; back, 27; chest, 15; rectum, 11; and vagina, 4. Five did not complain of any radiation of pain.

Nausea was the most frequent general symptom (162 cases). Vomiting was next (140), followed by weakness (133). Fainting was the least frequent but did occur in more than one-third of the cases (91). When fainting did occur, the diagnosis of ectopic pregnancy was usually correct. In the cases studied, there were only 3 instances of actual fainting in whom no ectopic was found. It is very important to note that no general symptoms were present in 32 instances. In 56 cases there was a definite history of frequency and dysuria associated with the onset of the symptoms. Half of this number (28) presented bowel symptoms, particularly pain on defecation.

Although more than half of our cases (160) were admitted to the hospital 50 or more days after their last menses, 56 cases sought admission 30 days or less from the time of their last menstrual period. It is difficult to ascribe a clear-cut pattern to the type, duration, and amount of bleeding in our series of ectopics. Bleeding varied from spotting of only a few hours duration to many weeks, many times with an interval of no bleeding. The quantity was from scanty to fairly brisk hemorrhage with all gradations between. Very few cases gave a history of having passed a decidual cast. In 41 cases the bleeding was continuous with the last menstrual period. In 9 cases there was no bleeding whatsoever. Pain was experienced within less than 20 days from the last menses in more than 75 per cent of our series. There were 60 cases in which pain began with the last menses and continued more or less. In 6 instances only was there no pain present. It is difficult to correlate the occurrence of the pain with that of the bleeding, since both were variable.

A temperature of over 101 degrees was uncommon. A pulse rate of over 120 on admission was infrequent, in spite of the fact that 130 patients had 500 cubic centimeters or more of free blood in the peritoneal cavity, and 35 patients were in surgical shock. There was nothing significant about the respirations. In more than two-thirds of the cases, the blood pressure was normal. There were 35 instances of shock.

Distention of the abdomen was present in one-third of the cases. An abdominal mass was felt in slightly more than one-tenth of the cases. Tenderness was noted in both lower quadrants in more than one-third of the patients, generalized tenderness in slightly less than one-fourth the number. In slightly less than one-fifth, there was no tenderness. Cullen's sign was reported only twice, although looked for constantly. The cervix was

tender on motion in approximately two-thirds of the cases. The uterus was normal in size and position in approximately the same number. In more than three-fourths of the patients an adnexal mass was palpable and nearly always tender. In more than half the cases there was fullness or a boggy or doughy mass in the cul-de-sac which was practically always tender. The size of the adnexal mass varied from 4 centimeters to 8 centimeters, rarely more.

Unfortunately in more than one-third of the cases a red blood cell count was not done. In 199 cases in which the red count is reported, 160 had a count of 3,000,000 or more, and in only 5 cases was the count less than 2,000,000. In 250 cases the hemoglobin was 60 per cent or more. More than one-third of the patients had a white blood count within normal limits, and in another third, the white blood count ranged between 10,000 and 16,000. In less than one-fifth of the cases did the white blood count go over 16,000. The differential count showed 70 per cent to 80 per cent polymorphonuclears in one-third of the cases, and in more than one-third, 80 per cent to 90 per cent. In only one-tenth of the cases were the polymorphonuclears 90 per cent or more.

In approximately two-thirds of the cases, the sedimentation rate was 60 minutes or over (Linzenmeier). In one-fifth of the cases the rate was 30 to 60 mintues. In only a small group, less than 8 per cent, was the sedimentation rate less than 30 minutes. It is important to note that where the sedimentation rate was 30 minutes or less, the diagnosis of ectopic pregnancy was usually not confirmed at operation.

In those cases in which the diagnosis is not obvious and the symptoms do not demand immediate operation, we feel that the Aschheim-Zondek test is of the greatest aid in arriving at a correct diagnosis. The test was done in 69 cases, and suggested but not done in 6 cases. In 50 instances the test was positive, and in 19 cases it was negative. Of the positive cases, 45 were ectopics, 3 normal pregnancies, 1 complete abortion, and 1 chronic salpingitis, all of which were operated upon for ectopic pregnancy. It was noted that in our series there was only 1 false positive (2 per cent). Of the 19 negative tests, 6 were not ectopic (32 per cent), and 13 were ectopics. Of these 13 ectopics, 5 gave a history of bleeding more than 6 weeks. In those cases in which the test was suggested but not done, half were ectopics, (3 ectopics and 3 not ectopics). Excluding abortions and normal intrauterine gestation, in doubtful cases a positive Aschheim-Zondek test always means ectopic pregnancy. The converse, i.e., a negative Aschheim-Zondek test is not true, for an old ectopic may be present with a negative test, depending on the time elapsed from the onset of symptoms to the performance of the test. However, in the face of a negative Aschheim-Zondek test, one must be more cautious in making the diagnosis of ectopic pregnancy for the chances of error are about one-third (6 in 19 cases or 32 per cent).

TABLE I.—ACCURACY OF DIAGNOSIS COMPARED WITH ASCHHEIM-ZONDEK TEST

	1930	1931	1932	1933	1934	1935	1936	Total
Positive Aschheim-Zondek	0	7	7	4	6	14	12	50
Ectopic	0	7	5	4	6	12	11	45
Not ectopic	0	0	2*	0	0	2†	1*	5
Negative Aschheim-Zondek	0	2	1	1	7	6	2	19
Ectopic	0	1	1	1	5	4	1	13‡
Not ectopic	0	1	0	0	2	2	1	.6§

*These 3 patients diagnosed as positive ectopics were normal pregnancies.
†These 2 patients diagnosed as positive ectopics proved at operation to be 1 case of complete abortion and 1 case of chronic salpingitis.
‡Five patients of these 13 ectopics gave a history of bleeding more than 6 weeks.
§Five of these patients had salpingitis and 1 had an ovarian cyst.

Of the 240 ectopics, 84 had less than 500 cubic centimeters of free blood in the peritoneal cavity, 96 had from 500 to 1,500 cubic centimeters, and 34 had over 1,500 cubic centimeters. It is interesting to observe that only 35 of these patients were in shock on admission or any time prior to the operation. Our table includes all operative cases (310), all of which were not ectopics. This explains the large number (92) with no free blood in the peritoneal cavity.

The fundus was normal in size in nearly twice as many instances as it was enlarged, and then only slightly enlarged. In about 10 per cent the uterus was retroverted; the re-

mainder were normal in position. The right tube was involved in 130 cases, the left tube in 110. The opposite tube was seen to be normal twice as often as pathological (145–71).

Colpotomy was performed only 4 times, and curettage 14 times. The curettage, however, was misleading in nearly half of those cases in which it was done, a diagnosis of incomplete abortion being made, and the patient allowed to return home only to be readmitted with a ruptured ectopic; or a curettage was done for incomplete abortion and a diagnosis of ectopic pregnancy made; the patient was then subjected to a laparotomy and salpingitis was found at operation. In 127 cases 1 tube was removed, in 92 cases 1 tube and 1 ovary was removed. An attempt is made, whenever possible, to leave the ovary on the side involved.

There were 20 single transfusions and 1 double transfusion before operation. Forty-nine patients received 1 and 5 received 2 transfusions after the operation. In all, 99 transfusions were given. There were 58 postoperative complications of which 24 were wound infections and 17 pneumonia. These comprised the majority of the complications.

More than half of our patients were in the hospital less than 3 weeks. Only one-sixth of the cases were hospitalized 25 days or more. Eight patients of the 310 operated upon died. One-half died from hemorrhage and shock either on the operating table or a few hours after operation. During the last 3 years of our study no deaths occurred. It is interesting that although pulmonary embolism occurred 5 times, only 1 patient died from this complication. Pneumonia, which was present in 17 cases, caused only 1 death (Table II).

The importance of anesthesia, both as regards method and administration, must not be overlooked. The use of cyclopropane in recent years by a well organized and efficient anesthesia department has resulted in the saving of many lives. We attribute this to the careful selection of type of anesthesia and efficiency in the administration of it.

The most frequent difficult differential diagnosis is that of chronic salpingo-oophoritis. The diagnosis of ectopic pregnancy with this finding at operation is almost 3 times as frequent as the reverse. In these cases where the diagnosis is difficult we feel that the Aschheim-Zondek test is indispensable.

TABLE II.—MORTALITY CAUSES

Year	Number	Cause of death	Time elapsed after operation
1930	1	Pulmonary embolism	5 days
	1	Hemorrhage and shock	4 hours
1931	1	Hemorrhage and shock	1½ hours
	1	Hemorrhage and shock (on table)	3 hours (after admission)
	1	Hemorrhage and shock	17 hours
	1	Acute mania (temperature 110°)	14 hours
1932	1	Paralytic ileus	4 days
	1	Postoperative pneumonia and distention	9 days
Total	8		

A total of 2,408 laparotomies was done, 310 of which were performed for ectopic pregnancy. Of this number 218 diagnoses were correct while 92 were wrong. Seventy patients diagnosed as ectopics revealed the following at operation: acute salpingitis, 20; chronic salpingitis, 31; ovarian cyst, 5; normal pregnancies, 6; appendix, 1; parametritis, 1; retroversion, 1; incomplete abortion, 1; postoperative adhesions, 1; rupture of broad ligament, 1; and no gynecological pathology, 2.

Twenty-two patients were diagnosed as follows, but at operation ectopic pregnancy was found: acute salpingitis, 1; chronic salpingitis, 11; ovarian cyst, 4; fibroid tumor, 2; surgical abdomen, 1; acute appendix, 1; endometritis, 1; and threatened abortion, 1. Twenty-six operations performed were necessary while 66 operations were unnecessary.

As has been previously shown, more than two-thirds of our cases occurred in the ampullary portion of the tube. More than half of these were internal ruptures. There were only 10 interstitial pregnancies, and these all ruptured externally. There was only 1 ovarian pregnancy, and this was primarily in the ovary. This case was studied and reported by Doctor Studdiford.

There was microscopic evidence of inflammation in slightly more than half of the ectopics, chronic inflammation being by far the most common finding (114). We have no

definite record of abscess formation due to secondary infection in a single instance. In somewhat less than one-third of our cases (73), there was no pathological evidence of inflammation. Although endometriosis, as a causative factor of ectopic pregnancy, has been emphasized by some writers, we were not able to substantiate this finding.

SUMMARY AND CONCLUSIONS

1. There is an unusually high incidence of previous lower abdominal surgery.

2. Although a history of pelvic infection was obtained in less than 20 per cent of our cases, microscopic examination of the tubes showed evidence of inflammation in more than 50 per cent.

3. Overemphasis has been placed on the sterility period prior to the occurrence of an ectopic pregnancy.

4. The number of previous pregnancies or their termination bear no relation to the incidence of ectopic pregnancy.

5. Pain is most often colicky, severe, irregular, and generalized over the abdomen. Radiation to one or both shoulders is relatively uncommon, but significant when present.

6. Nausea and vomiting are far more frequent than fainting. The latter, when present, is pathognomonic.

7. Pain and bleeding in relationship to the last menstrual period is extremely variable as to occurrence, duration, and amount, and often difficult to correlate.

8. Physical findings without laboratory aid are often misleading.

9. The sedimentation rate is most often normal in spite of an elevated white count.

10. In doubtful cases, the Aschheim-Zondek test (or Friedman modification) is indispensable. Excluding abortions and normal intrauterine pregnancies, a positive test always means ectopic pregnancy.

11. The use of repeated whole-blood transfusions before, during, and after the operation should reduce the mortality to less than 2 per cent.

12. The percentage of error in our series was 29.7. The commonest cause of error was chronic salpingo-oophoritis. This, we believe, can be greatly reduced by the more frequent use of the Aschheim-Zondek test.

13. More than two-thirds of the cases of ectopic pregnancies in our series occurred in the ampullary portion of the tube, as has been reported by other investigators.

14. Pathological examination of the tubes removed revealed inflammatory reaction both acute and chronic in over 50 per cent of the cases. The relationship this finding bears to the etiology and pathogenesis, we are not ready to state. Endometriosis as an etiological factor was not observed in a careful pathological study of our series.

A PRACTICAL AND CLINICAL TEST FOR LIVER RESERVE

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FROM a surgical standpoint it would always be important to know the working capacity of the liver, if it could be told. The value of such information is obvious. This is particularly true when it is a factor in the diagnosis and prognosis of such cases as pancreatic disease, affections of the intrahepatic or extrahepatic biliary tree, operations in the upper abdomen, and metastatic lesions of the liver. Such lesions, if they could be demonstrated, would indicate the possible futility of surgery. Its greatest value and application, however, is in the too often neglected and ignored liver dysfunction which is always a constant accompaniment of biliary tract and thyroid pathology. It is recognized by too few that disease of the gall bladder and thyroid is *always* associated with liver pathology, or at least with functional changes which produce a loss of reserve power. In fact liver pathology often precedes and produces gall-bladder trouble. Failure to recognize this fact is the cause of a great deal of the operative mortality in general practice.

Cholecystectomy is the second most common operation performed on the human, and yet the average global mortality is from 10 to 12 per cent with a high of 25 to 30 per cent and a low of 3 to 5 per cent. These figures are based on replies to an inquiry sent to hospitals in the smaller and medium size cities listed in the *Directory* of the American College of Surgeons. This death rate does not apply to the larger centers or clinics. However, the smaller hospitals and the general practitioners throughout the country do the greater amount of work, so that this is the mortality that should be considered rather than the mortality of specialists in teaching centers. Why is it that a condition so prevalent and whose operative treatment is rarely an emergency, should have a mortality so high? The answer may be found partly in the liver and partly in the heart—but the relationship of gall bladder and heart is another question! Certainly the liver is to blame in many instances. Even when a surgical death is due to hemorrhage, the liver is indirectly responsible. No other common surgical procedure carries such a high mortality except perforated appendix and this is associated with a peritonitis. The late Lord Moynihan once said that surgery has now been made safe for the patient, and that it remains for us to make the patient safe for surgery. We cannot be considered faithful trustees of our patients' future health if we do not realize this fact. If we do, we will always determine before operation (as well as we can) whether any particular liver may or may not stand the strain of operation, after operation.

Regarding the thyroid, it is a well known fact that the feeding of excessive amounts of thyroid extract to animals will completely diminish the store of glycogen in the liver cells, and also that the injection of blood from thyrotoxic patients will do the same thing. This is a partial explanation of why the so called liver shock death following gall-bladder surgery resembles so closely, and why some consider it the same as the thyroid crisis which also results in death. It shows too the importance of knowing liver function in thyroid patients, and why glucose therapy is of such value in thyroid surgery.

Every operative procedure undertaken, even the setting of a fracture or a tonsillectomy, is a potential death, but this applies particularly to operations on the biliary tract. *Every liver with a diseased gall bladder is damaged before operation, and every operation decreases the ability of any liver to function with the maximum reserve*—hence the importance of knowing how much of this maximum reserve is available in case of need. If the surgical mortality of this, and other conditions, is to be lowered, then everyone must be considered a potential death and liver reserve tests done on each one. In the presence of an abnormal response, as will be

shown, operation should be postponed until it is normal, or until an honest effort has been made to bring it to normal.

Crile has shown that a liver can lose from 10 to 15 per cent of its efficiency for each degree loss in temperature, and also that the loss at operation may, in rare and extreme cases, reach 3 degrees . . . so that there is a potential loss of 40 to 45 per cent of liver function by only opening the abdomen. This does not take into account shock, trauma, or anesthesia. If a liver can lose 40 to 45 per cent of its function by only opening the abdomen, and it may lose another 30 to 40 per cent by shock, trauma, anesthetic, and other incidental happenings at operation (a possible total of 80 to 85 per cent), then it is obvious that, if the loss of efficiency is maximal, there can be only one result if that liver has less than 85 per cent of its functioning ability to begin with (i.e. if it has lost more than 15 per cent, which is a very small amount). It fails completely, and death ensues almost at once. This paper will show how a new procedure may give definite information regarding the amount of liver reserve, probable or possible liver failure, and the optimum time for operation.

THE BROMSULPHALEIN DYE TEST

In a recent communication[1] I described a new technique for the dye (bromsulphalein) liver function test. The present report has to do with further observations on, and the standardization of, this new method. The old method of doing the test was as follows: The dye was injected into the circulation and the amount remaining at a stated time interval was determined. When a 2 milligram dose was used the estimation was made at 30 minutes, and when a 5 milligram dose was used 60 minutes was considered the normal. Recently 30 minutes has been considered the time limit for the larger dose too. If more than 5 per cent of the dye remained at that time it was considered pathognomonic of liver disease. Conclusive experimental evidence has shown that this dye is excreted solely by the liver. Part of this evidence is, first, 85 to 90 per cent can be collected within 1 hour after injection, by draining the common bile duct, and, second, hepatectomy produces 100 per cent retention.

Snell and McGath at the Mayo Clinic, where this test has been used over 10,000 times, say that it is the simplest and most valuable yet devised. McGath has shown that 96 per cent of the livers which show a retention are damaged. Bauman and Orr recently published a small series of cases from the New York Presbyterian hospital showing that 100 per cent of livers with retention had pathological processes as determined by section at operation or autopsy. Eusterman considers it to be the best test of liver function. Bourne and Rosenthal after studying the effects of different anesthesias on animals said "one result of our study was the conviction that the dye (bromsulphalein) test affords a much more definite index of injury to the liver cells than do estimations of bile pigments in the blood and urine." Relative to surgery Cantarow says that "for purposes of safety, all such individuals exhibiting any degree of dye retention should be regarded as relatively poor operative risks and, if possible, should be treated by more conservative measures until normal values are obtained." In short, it is the general consensus among authorities that it is the most practical, reliable, and valuable test for determining liver function in non-jaundiced patients. Its value in jaundice is less because the icterus of the serum changes the purple color of the dye and estimations are only approximate. Assuming that this dye test is of such value, as it is performed now, then any improvement over this method must be given serious consideration. This discussion is such a consideration.

The present method (i.e. the single determination) tells very little if the test is normal. It does not give any information about the actual length of time required for the liver to do a given amount of work, nor does it tell the efficiency with which it is done. But it is important to know this, because two livers, both of which have 0 per cent retention at the time limit, do not necessarily remove the dye in the same length of time and so cannot be the same in working capacity. One may do the work in 10 minutes and an-

[1]Canadian M. Ass. J., 1938, 39: 556.

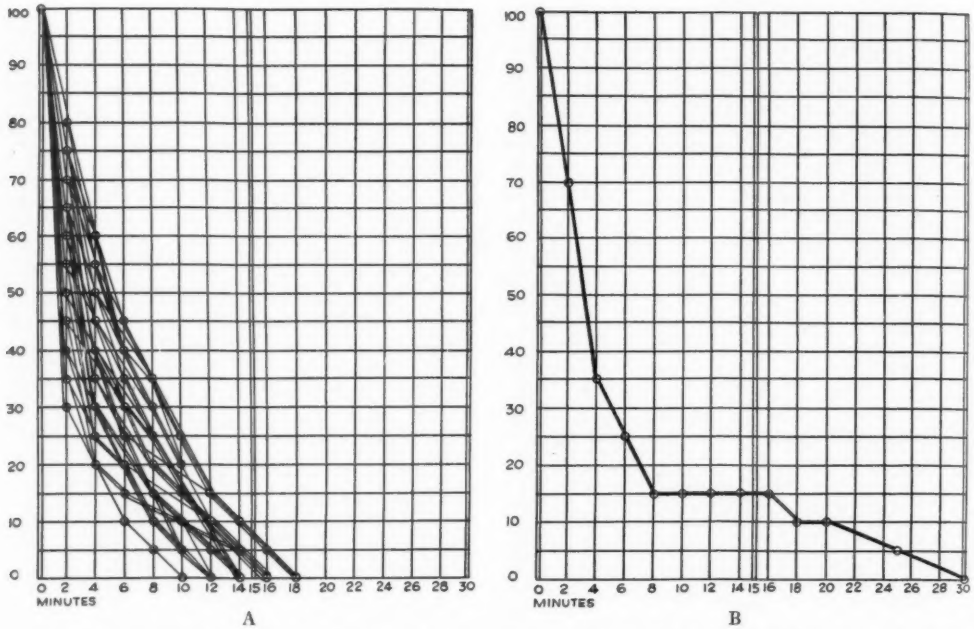


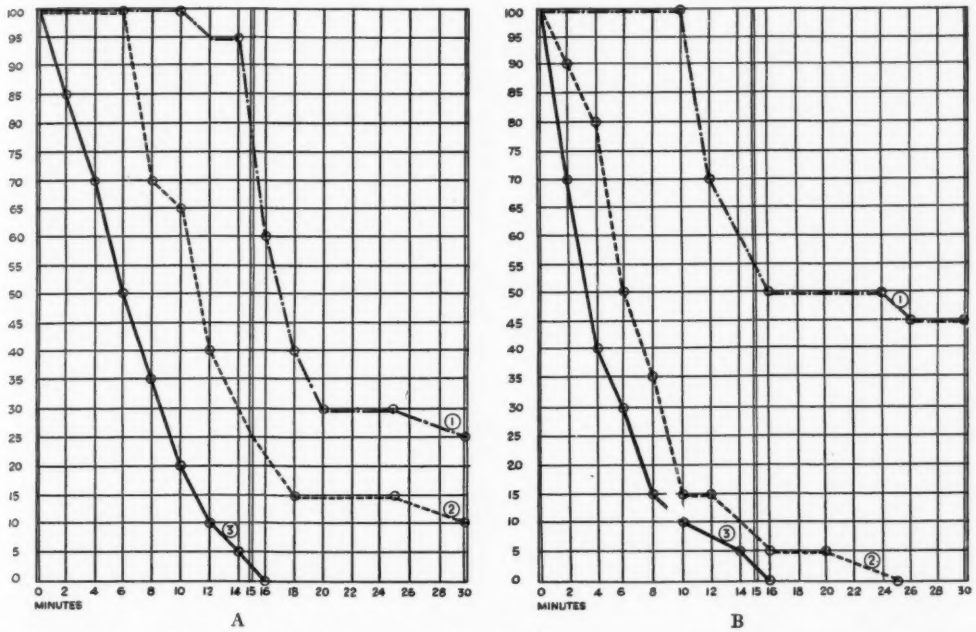
Fig. 1. This represents the curve produced by the apparently normal liver, using the 2 milligram dose. It is seen that the dye is removed evenly, continuously and with no hesitation. There is a constant and consistent disappearance from the blood. In this chart there are 35 normals superimposed on the same graph and the upper limits of normal are clearly defined. At 10 minutes there are only three which show over 20 per cent retention; at 12 minutes there is only one over 15 per cent; at 14 minutes none are over 10 per cent; and at 16 minutes none over 5 per cent. In contrast to this is the graph in Figure 1B which shows a marked difference. By the old method of determining the dye retention this result would have been considered normal because it showed no percentage retention at 30 minutes. But it is obvious that, as a working unit, it is much less efficient than the liver which produces a normal curve. It removes only 5 per cent of the dye in a 12 minute period. The diagnosis was carcinoma of the rectum.

other in 25 minutes, yet both results would be interpreted the same. An abnormal liver, with its tremendous reserve, can give the same results as a normal liver, if given time enough. And so it was thought that if the *rate* at which the liver removes dye from the blood could be determined, there might be produced a curve typical of the normal liver, and that if a normal could be established, then early and small amounts of liver changes could be told. This was done by estimating the remaining dye in the blood at 2 minute intervals and plotting a graph.

These graphs reveal two important facts: (1) They show that 18 minutes and not 30 minutes is required for complete removal in the normal. (2) All livers which remove 100 per cent of the dye inside the 30 minute normal time limit do not do so by having a consistently lower reading at each successive estimation. That is, the liver may not remove any dye at all for 2, 4, 6, 8, or 10 minutes and yet may remove it all within the previous normal time limit.

In comparing these curves it must be admitted that, as a working unit, a liver represented by the curve showing a consistent and continuous disappearance from the blood (Fig. 1A) is more efficient than a liver which removes only 5 per cent in 12 minutes (Fig. 1B). This difference, which could not be told by the single estimation, is evident in the curves.

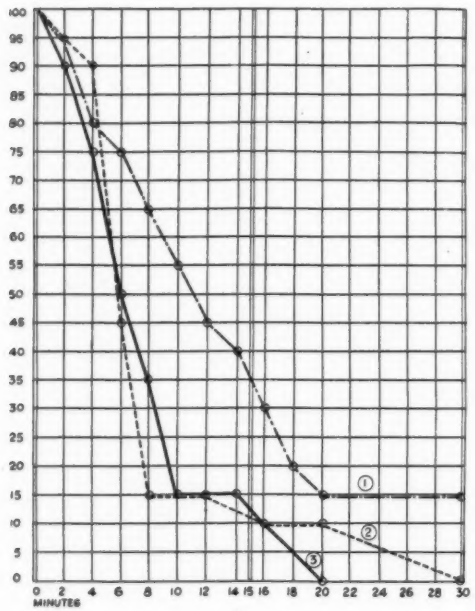
Also, it is well to consider this fact. If a liver hesitates, or has difficulty in removing a small amount of dye from the blood (Fig.



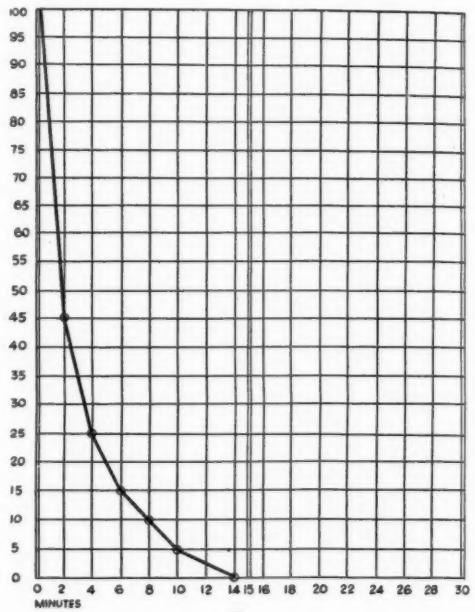
A B

Fig. 2. A shows the value this test is in pre-operative treatment. Curve *1* was made 5 days before operation for gastro-enterostomy. Curve *2* was made the day before operation and would be considered by the old method to be only slightly above normal (10 per cent retention). He received continuous 2½ per cent glucose in hypertonic saline for the intervening 4 days. (The feeding of sugar does not make any difference to the curve unless there is a definite deficiency, as there is here.) Postoperatively this man had a "rough" time, and had he not had more good liver than there was when the first curve was made, he may not have survived. If, however, he had waited for operation until the liver was normal, as shown by curve *3*, which was done 2 weeks after operation, he may have had an uneventful recovery. This illustrates reserve and not damage. The liver's working ability was made normal by proper treatment. The first graph represents a liver "all tired out" which is unable to do any extra work. Curve *3* is made of the same liver rested and fresh, ready for work. It is certainly better able to do work than the first—why, then, should every person whose liver may be called on to do any extra work not be prepared and given the best liver ability possible? A liver should be given all the time necessary to get "built up" before subjecting it to the strain and extra burden consequent upon surgery. No one can tell when it may be needed. B, Hysterectomy was performed. The second postoperative day the patient's pulse, temperature, and respirations increased. There was no apparent reason for this. Her liver curve (curve *1*) was bad. Had this loss of efficiency been added to an abnormal curve (Fig. 2A, *1*), it is easily conceivable that failure might have occurred. Hence the importance of having a normal liver. Curves *2* and *3* look alike but actually there is a big difference. Curve *2* shows a great improvement (*2* days later) and curve *3* is normal (*1* week later). At 4 minutes it has removed 40 per cent less dye than in curve *3*, but they are both within the 30 minute time limit and by the single estimation both would be considered to be the same and normal. The curves, however, show this fallacy.

1, B) will it not of necessity encounter a great deal more difficulty in "looking after" the postoperative toxic products, and will it not have real trouble handling shock, trauma, and anesthesia? Indeed, is it not possible that such a liver would be unable to do this extra work and that it may fail? Such a supposition is illustrated by a man who had a partial pyloric stenosis. His liver function was bad (Fig. 2A, *1*) on admission to the hospital but it was improved by 5 days' treatment (Fig. 2A, *2*). Gastro-enterostomy was performed before his liver curve was normal because he refused to wait any longer. Recovery was very eventful. For 24 hours his postoperative course was normal and then he "went bad," became irrational and comatose, his pulse and temperature increased, and urine decreased with albumin 2 plus. Recovery was not assured until 3 days later, and it is suggested



A



B

Fig. 3. A, This illustrates the improvement in gall-bladder disease of 15 years' standing. Curve *1* was made before an acute empyema was drained, and curve *2*, 2 weeks later. The fistula continued to drain bile, and was therefore producing a gradual decompression of the liver. This had a good effect as shown by curve *3*. Operative complications will be much less with a curve like *3* than they might have been had operation been done with a curve like *1*. Why then, should all potential biliary tract surgical cases be not drained duodenally? B, Diagnosis—chronic cholecystitis in a girl of 12 years of age. The liver shows no damage as determined by the dye retention. This is likely because the condition has been present for a short time, and because all young people have such a great amount of liver reserve. This curve indicates a good operative risk. Postoperative course and subsequent health were excellent.

that if his liver had not been improved before operation, recovery may not have taken place at all. No doubt the available good liver was of great help. Had operation been postponed until the curve was normal (Fig. 2A, *3*), it is likely that recovery would have been less disturbed. Hence the conclusion seems definite that every person should have his liver function improved before operation, and if improvement cannot be made then complications should be looked for and prepared for. Such an improvement in gall-bladder cases is seen in Figure 3A and the value of a normal liver, before operation, in Figure 2B. If this patient had not had a "good" liver before operation, she might have encountered great difficulty with the loss that she suffered. Curve *1* represents the loss after operation. If she had a curve as Figure 2A, *1*, and the loss after operation had been added to that instead of to a normal, failure might have resulted.

Young people with cholecystitis usually have not had the disease long enough to produce liver changes, and also, the younger a person is the more liver power they have. This is seen in Figure 3B, which is the curve of a girl 12 years of age. Operation and pathological report proved that the diagnosis of chronic cholecystitis was correct. Her recovery and subsequent course were excellent. If she had been allowed to progress for 10 or 20 years, liver damage may have been marked and surgery less successful. Gall-bladder pathology should be thought of more often in 'teen age patients. I do not think that this disease (either pathological or clinical) appears for the first time in the forties, or even in the thirties. It is more often "passed up"—

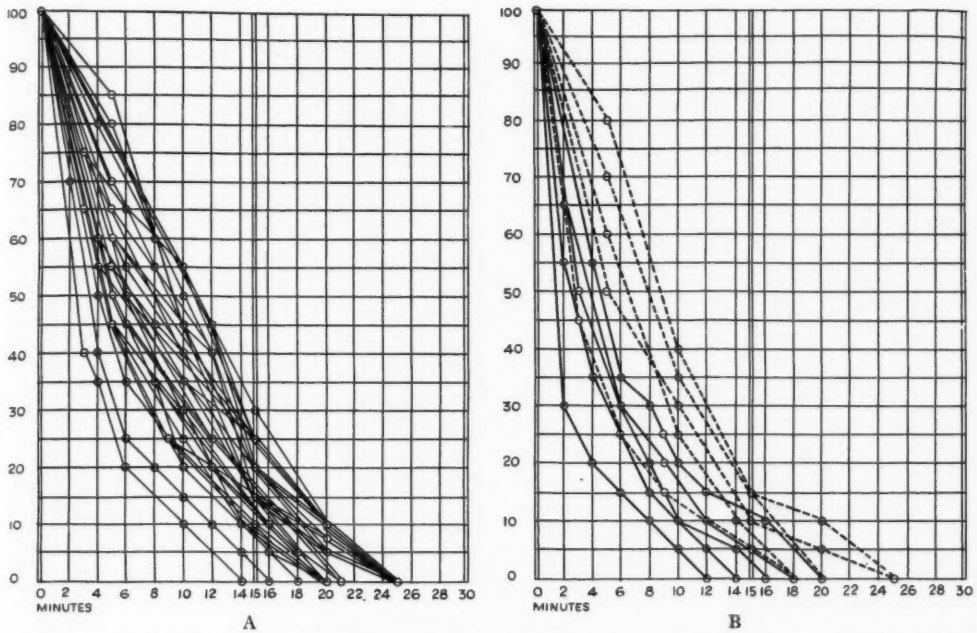


Fig. 4. Twenty-five normal curves picked at random. The dose was 5 milligrams per kilogram and all are out in 25 minutes with the same type of curve as was produced by the 2 milligram dose. In this case the liver has 2½ times as much work to do as with the smaller dose, but it does it in approximately the same length of time. This is illustrated in B where the straight line represents the 2 milligram dose and the broken line the 5 milligram dose. These show that in some cases the larger dose is removed in a shorter time than the smaller. From this it is evident that the 2 milligram dose does not put a very great load on the liver and is not a satisfactory test for that reason. The 6 milligram and the 10 milligram doses require 35 and 60 minutes, respectively, for removal. Therefore the 5 milligram dose is the largest that will give the curve as represented by the normal, which is all out in 25 minutes at the maximum. It does therefore put a maximum load on the liver.

and a wrong diagnosis made, if one is made at all—in earlier life when a correct diagnosis could have been made if only considered. And conversely, in adult life, the gall bladder is many times "sentenced" as guilty, when it is actually innocent.

LIVER FUNCTION

In structure, the liver is the least complex organ of the body. In function it is the most complex and the least understood. Its functions are many and varied and seem interchangeable one with the other. They are even able to be taken over by other units of the body in times of need, and it can carry on normal function with only 20 to 25 per cent of the parenchyma intact. Some investigators have reportedly removed as much as 95 per cent of the liver in experimental animals before loss of function became evident. This tremendous reserve applies to its main secretion also, the bile, which can maintain normal intestinal activity with only one-fifth to one-tenth of its normal amount. Hence the difficulty in finding a satisfactory method of testing this organ normally or in disease.

There are only three types of cells in the liver: those lining the bile capillaries, the Kuppfer cells lying along the blood channels (sinuoids), and the liver cell proper which lies between and forms the only thin partition separating these two canals.

These liver cells proper are the ones which really do all the work. Among other functions they metabolize, store, secrete, detoxify, and excrete. They are the most important

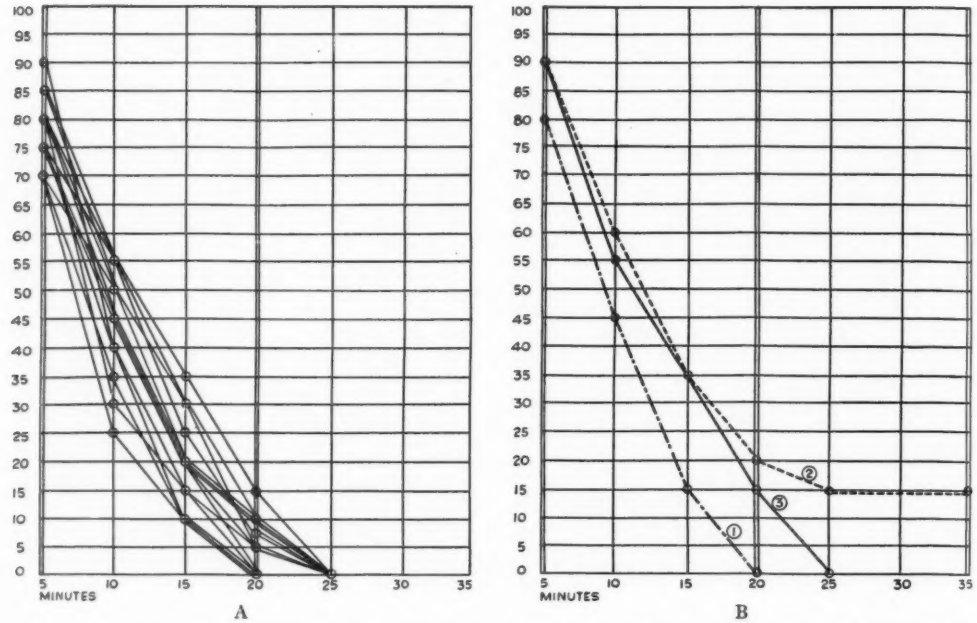


Fig. 5. A, represents the curves in what is considered to be a liver which functions with a maximum reserve power. The first 5 minutes of the chart have been taken off which leaves an extra 5 minutes at the end. The dye is removed consistently and it produces an even curve. This is the present normal. B, illustrates how the liver loses some part of its maximum efficiency by an operation. Curve *1* was made one day before a simple cholecystectomy was performed, and curve *2* was made 24 hours later. This is not a marked removal from the normal, but it is moderate in view of the easy technical work that was necessary and the short time taken. Curve *3* was made 1 week later and shows the liver back within the normal range. Diagnosis was "cholelithiasis of metabolic origin."

cells in the organ as they take part in nearly every function. Because of this it seems reasonable to assume that if a dependable method can be found to tell *any* early deficiency of these cells in *any* function it would be of value —and that the earlier it could be told the better. If these cells are working below normal in any one function, regardless of which function it may be—they may well become deficient in other functions also, and for safety sake it should be assumed that such a deficiency will occur. Then proper precautions can be taken. *Any loss of the liver's normal ability must be considered seriously and demands careful second thought before surgery is undertaken.*

To provide a test of value, a heavy burden must be put on some function which will make it work at a maximum to give the normal result. If any working unit is working with its maximum strength, using all of its reserve to give a normal result, then any loss of this reserve can more easily be seen. The repeated determinations of the dye retention depends on this theory. To find out if there is a loss of reserve is all important. When reserve in any organ—heart, liver, kidney, or lung—is lessened, that organ has a greater chance of failing. Tests then should be tests of reserve rather than of function. The ability of the liver to work under pressure, that is after operation, is directly proportional to its reserve. Hence the imperativeness of knowing the relative amount of this reserve. A test, to be of value, should give information regarding the amount of reserve that can be called upon in case of need before function actually starts to fail, and the amount of extra liver that can be used in an emergency, as is told by kidney reserve tests. Until all this

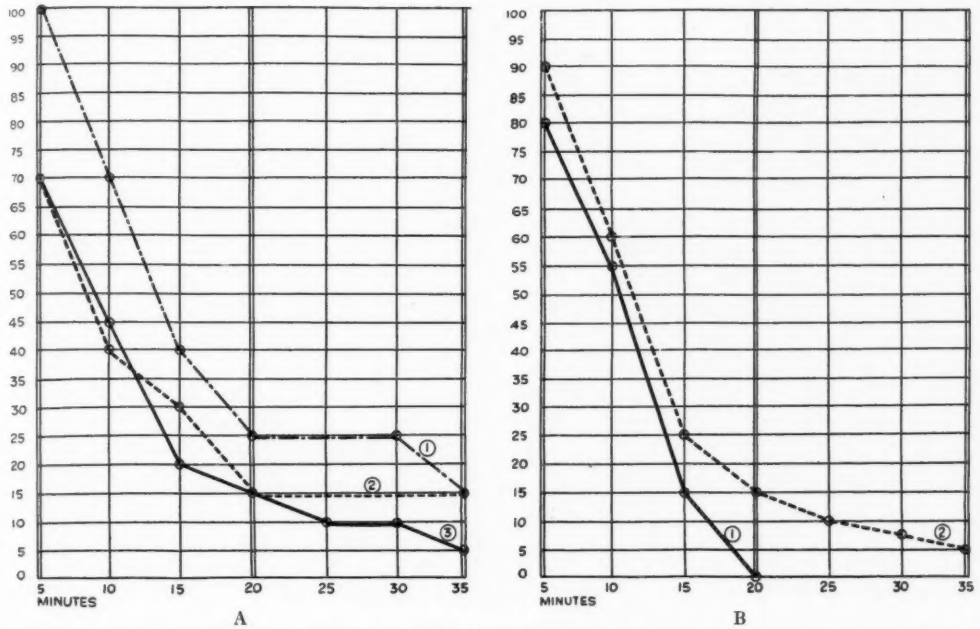


Fig. 6. A is the chart of a man with a diagnosis of gastric ulcer. Because of his liver involvement, as shown by curve *1*, malignancy was considered. Six weeks later, however, after a marked clinical improvement the curve *2* was done, and shows also just as marked an improvement in the liver efficiency. This illustrates very well the improvement over the old technique. In this instance both of these results would have been interpreted the same because they both had the same retention at the time limit. But it is obvious that the second is a great improvement over the first. Curve *3* was taken 3 weeks later, and shows continued improvement. At the present time this would seem to indicate the absence of malignancy because if the first curve was bad due to metastasis, it likely would not have improved as readily as it did. In this particular case, it is then a great value in diagnosis and prognosis. B shows the value in prognosis. The first curve was made a day before radical mastectomy was done for carcinoma. Curve *2*, done 3 months later, shows the liver less efficient. If this deficiency increases it is evident that the prognosis is not as good as it would be if the curve did not become abnormal. This is an illustration of the possibilities of the improved technique.

"extra" or reserve is used up there is no loss of function. This is the reason tests of liver function give so little information. A test of function will be abnormal only after that particular function is actually failing, and this does not fail until all of the reserve is used. A liver function test will give the same result whether there be 1 or 100 per cent of reserve, and such a test is of very little help when help is needed. This reasoning made it seem probable that even the graph made by the 2 milligram dose could be improved by finding out the largest amount of dye that would give the same graph. Consequently 4, 5, 6, and 10 milligrams per kilogram of body weight were used.

It was found that the 5 milligram dose required only about 5 minutes longer to be removed than the 2 milligram dose, and that in some instances it was removed in a shorter time (Fig. 4A and 4B). From this it is obvious that the 2 milligram dose does not put a maximum load on the liver. The 10 milligram dose on the other hand required 60 minutes to be completely removed from the blood and the 6 milligram dose about 35 minutes. The conclusion therefore appears definite that 5 milligrams of the dye per kilogram of body weight fulfills the requirements, namely, that it does make a liver use all of its reserve to give a normal result. The other two requirements of any such test are already

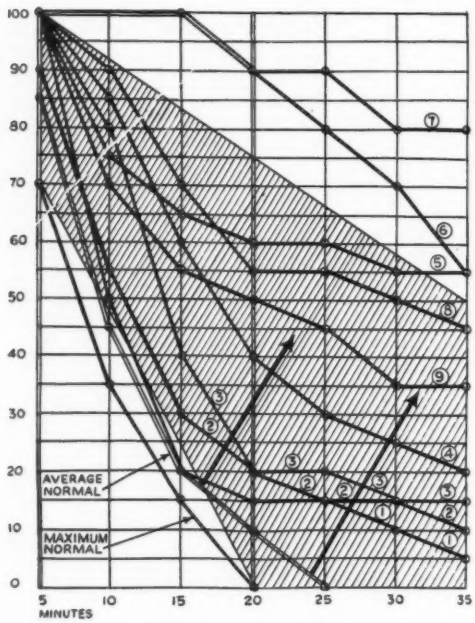


Fig. 7. This is a composite chart showing the theoretical value of this test. Curve *1* is that of a mild acute cholecystitis—first attack—32 years of age. Curve *2* is that of a young boy 21 years of age who has had two attacks of biliary colic, one of which was followed by jaundice. Clinically this case should have more liver damage than the first and the curve bears this out. Curve *3*, still a little further away from the normal, is a man of 45, who has had three attacks of colic each one followed by jaundice. Curve *4* is that of a lady 57 years of age who has had gallbladder "trouble" for 20 years. Curves *3* and *4*, besides showing a retention at 35 minutes have a high retention at 10 minutes. This is of great importance and if two curves, both with the same retention at 35 minutes, have definite retention at 10 minutes and 15 minutes, the one with the higher retention has the less efficiency. This is shown very well in curves *5* and *6*. Here both curves have 55 per cent at 35 minutes. By the old method these would have been considered to be the same and to be equally efficient. Curve *6* has at 15 minutes 100 per cent retention, whereas curve *5* has only 65 per cent. Curve *6* also has actual loss of function, as shown by the blood bilirubin of 1.5 milligrams. Curve *5* has a maximal normal bilirubin (0.25 milligram). Curve *7* also had actual loss of function (bilirubin 3.0 milligrams). It will be noticed that as the curve moves away from the normal curve it approaches closer to the point, which is inconstant, where the reserve has completely disappeared and actual loss of function supervenes. That point is some place between the group of curves *1*, *2*, *3*, and *4* and curve *7*, approximately around *5* and *6*. It is true then that as the curve moves toward this point it represents a liver with a diminishing reserve. Curve *5* has a maximum normal amount of bilirubin in the blood—0.25 milligram. This then represents a liver with no reserve whose function is going to start to fail almost at once.

fulfilled. They are: (1) that the dye is excreted by the liver only and (2) that estimations of the remaining dye can be made with relative accuracy.

The next step in improvement was to start the graph at 5 minutes and make estimations at 5 minute intervals instead of 2 minute intervals (Fig. 5A). The longer time interval allows of more accurate color determinations, and the first 5 minutes are deleted because they show nothing, this part of the graph usually being the same. It also leaves an extra 5 minutes at the end of the graph in case of disease. This curve is now considered the normal standard.

CLINICAL CASES

The clinical application of this test in the diagnosis and prognosis of cases is shown in Figure 6A. This is the chart of a man with the diagnosis of a gastric ulcer. Because of his liver involvement, malignancy was thought of. The first test was done before treatment was started. After 3 weeks' treatment his clinical condition had improved very much and 6 weeks after the first curve was made, a second was done. The interesting point is that at the final reading of the first two there was 15 per cent retention at both tests. But it is evident that the second curve is a great improvement over the first. This could not have been seen by the old method of determining the retention because both curves would have been interpreted in the same way, as both had the same retention at the time limit. The new technique herein described shows the great advantage of the graph. The third curve, 3 weeks later, shows continued improvement and indicates a good prognosis and the probable absence of malignancy. If the abnormal early curve was due to secondary growths in the liver, the curve would not likely improve. The change then is functional. In Figure 6B the prognosis can be determined with more accuracy than has heretofore been possible. Figure 6B, *1* was made one day before radical mastectomy was performed for carcinoma of the breast. The second curve was made 3 months later and shows definite increasing liver deficiency. This loss of liver efficiency is due either to metastasis, anemia

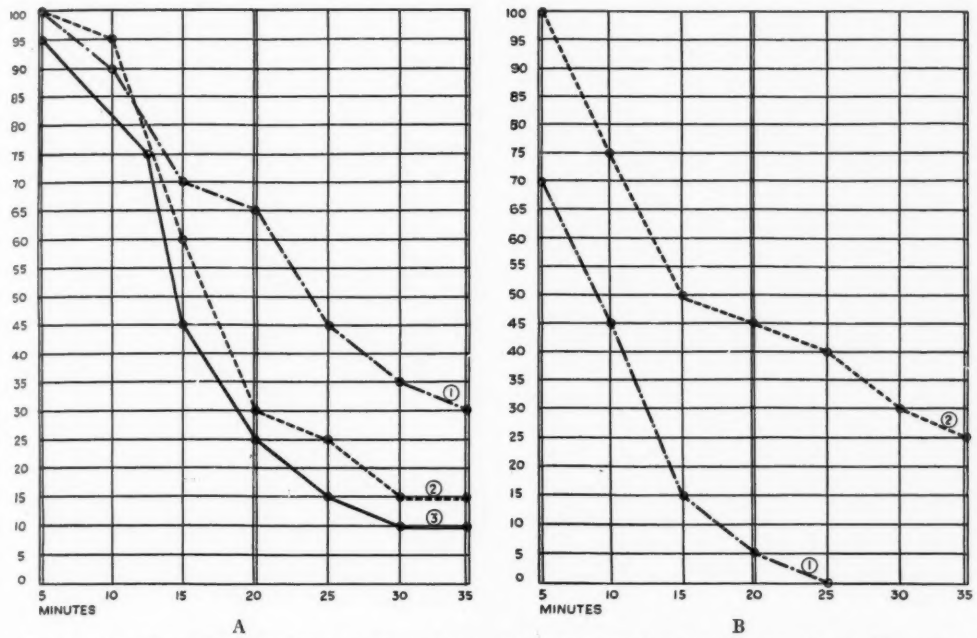
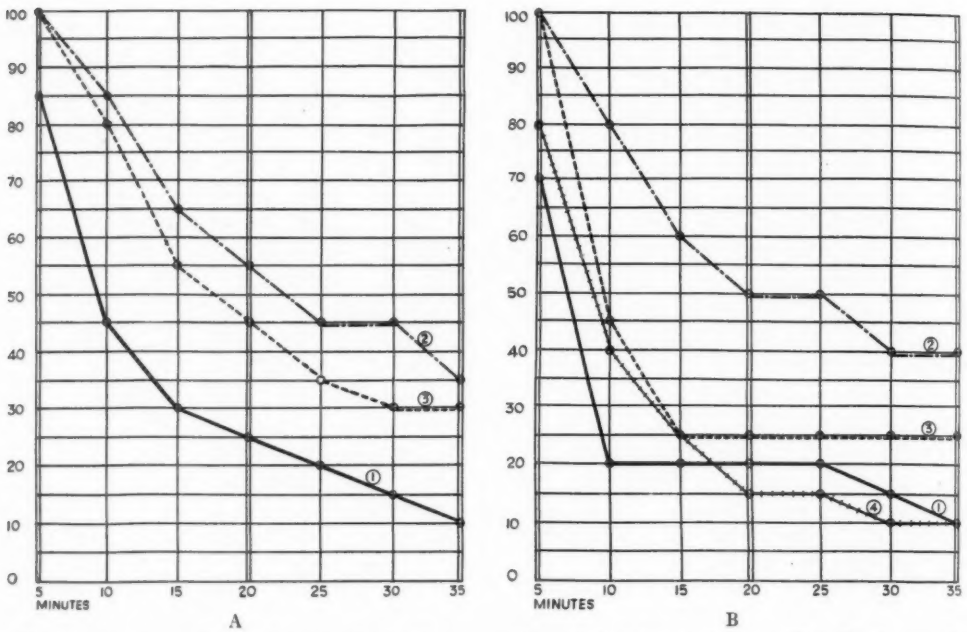


Fig. 8. A is a chart with three heart conditions all of which have no increase of bilirubin in the blood or urobulin in the urine. They all represent poor operative risks and illustrate the type of case which should be improved before operation. B, Curve *1* was made 1 day before mastectomy for carcinoma of the breast. The curve is perfectly normal. Curve *2* was made 24 hours later and shows a very marked loss of efficiency. This may be more likely due to anesthetic (cyclopropane) than to the operative procedure itself. It shows too, that if an operative procedure outside the abdomen can lower the liver reserve so much, then intra-abdominal surgery, particularly in the vicinity of the liver, may of necessity lower it much more, and this may reach the point of danger, especially if the normal reserve is not present before operation is carried out.

or cachexia. Whatever the reason it is apparent that the liver reserve is continually becoming less. Curves made at 3 month intervals will indicate, better than tests at present in use, whether liver reserve is decreasing or staying stationary, and by this her prognosis can be judged.

The proof that the liver loses some part of its maximum efficiency after operation is shown in Figure 5B. The first curve was made before operation for cholecystectomy. The second curve was made 24 hours after, when the maximum postoperative liver changes are present, and the third curve 1 week later, by which time it has returned to normal. This loss is not marked. The procedure was technically simple and the operation time 45 minutes. The patient was only 31 years of age and her reserve was good, as shown by a normal curve preceding surgery, which indicates little if any liver involvement. X-ray examination showed 2 stones but because the concentrating power was good, the emptying normal, and biliary drainage showed no pathology, it was thought that the stones were metabolic in origin. This would explain the small loss of liver reserve. Apparently the better curve a person has to begin with, the less is the loss of liver reserve.

The value of the bromsulphalein curve in the estimation of liver reserve is shown in Figure 7. Here curves *1*, *2*, *3*, and *4* all show no urobilin in the urine, and no increase of bilirubin in the blood, i.e. there is no loss of liver function as told by the present accepted early tests—but these curves show a very definite removal from the normal. Curve *7* on the other hand, shows urobilin in the urine



A B

Fig. 9. A, Curve *1*, 4 hours after operation for the removal of a large ovarian cyst. Curve *2*, 24 hours after operation; curve *3*, 48 hours after operation. B, Female, aged 45. Curve *1*, taken just before operation for cesarean section. (All pregnancies show a loss of liver reserve which is greatest in the ninth month.) Curve *2* is 22 hours after and shows the increased loss due to operation and anesthetic (ether). At this time she had a moderate upper abdominal distention; pulse 140; temperature 99.4 degrees. A diagnosis of acute gastric dilatation was made. Forty-four hours after operation the third test was done and revealed an improved liver. Clinically she was the same and because of the improved liver function a good prognosis was given. At 72 hours (curve *4*) the liver showed continued improvement. This is a graphic illustration showing how the liver can and does change its working ability through a wide range before any loss of function is produced. In other words, it shows how much extra work the liver can do in case of emergency. This has been a clinically accepted fact for some time but it has never before been shown graphically.

and an increase of bilirubin in the blood. This is associated with an actual loss of liver function, and it is seen, therefore, that the further a curve moves away from the normal standard, the more the reserve decreases. This decrease of reserve will continue until loss of function actually begins, and the relative amount of reserve left before function will start to fail can be told from the graph. At some inconstant point between the lower group and curve *7* reserve is completely used up and loss of function begins. This point is approximately at where curves *5* and *6* end.

Curves *5* and *6* are of great interest. Both have 55 per cent retention at the 35 minute mark, but the former has a loss of function as shown by a bilirubin of 1.5 milligrams and the latter has no loss of function as shown by the blood bilirubin of 0.25 milligram, which is the maximum normal. Although the last part of the curves are the same, and the previous interpretation would indicate that they had the same working ability, the first parts are very different. This early part is of importance in evaluating liver reserve. At 15 minutes the upper curve, *6*, still had 100 per cent retention and the lower, *5*, 65 per cent. Retention in this first part of the curve is of more importance than in the latter part, and indicates more loss of reserve than it does in the last part.

Function tests will show nothing abnormal until that function fails, but the improved technique will show liver changes before the

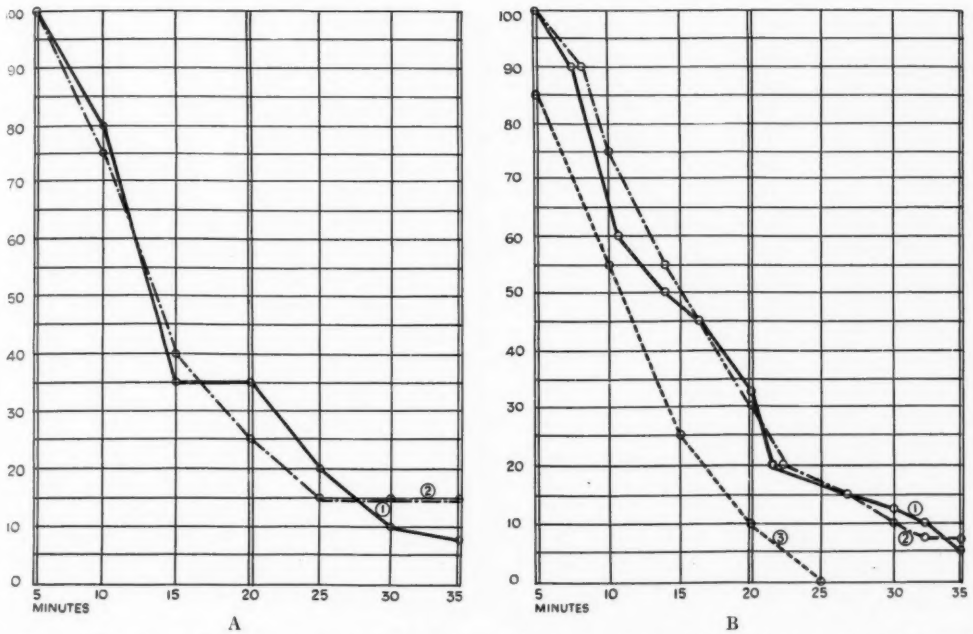


Fig. 10. This shows that the liver does not lose its maximum efficiency directly after operation. A, *2* is 2 hours after a strangulated hernia was repaired. The patient, a man 79 years of age had a spinal anesthetic. The curve before operation was abnormal which would be expected in a man of his age. B (*1* and *2*) are graphs made 1 hour before and 1 hour after operation for a twisted ovarian cyst. The patient was a girl 27 years of age and was suffering from a moderate degree of shock. She had a spinal anesthetic. In this case also the pre-operative liver efficiency was decreased as shown by the curve, and this is doubtless due to the presence of shock. Three weeks later the curve was normal. Compared with Figure 9 it appears that the loss is maximum between 18 and 36 hours. This is the time at which liver deaths occur! What is the relationship?

accepted tests of function are abnormal. By this you can estimate rather accurately how much reserve there is in store before function will fail. This estimation is of the utmost importance in surgical cases. Also, it is readily seen how this reserve increases and decreases, hence its value in diagnosis and prognosis, because the prognosis cannot be good in the presence of a curve moving away from the normal, nor can treatment be considered successful under the same circumstances. Differences in rate indicate differences in efficiency, and if changes in liver efficiency, for either the better or the worse, can be told, the prognosis can be judged so much better.

TECHNIQUE

The technique is simple. One venipuncture is sufficient for taking all the blood samples. The needle (short bevel and 18 or 20 gauge) is inserted as for a Wassermann. It is left in the vein and a Luer 3-way spinal monometer valve is connected to it, on one arm of which is a tube leading from a jar of saline (Fig. 11, *1*). With practice it is more convenient to insert the needle and valve together as shown in the illustration. With the handle in the position shown it is just as easy to tell where the needle is in the vein, as it is when the needle is joined directly to the syringe. The Baxter intravenous jar is used because it is so convenient for office use. Five hundred cubic centimeters will last for at least three patients. When the fluid, controlled by clamp, *3*, is running satisfactorily as told by the vacuum drip, *2*, the measured dose (5 milligrams per kilogram body weight) is injected slowly in any other vein so that the dye will

Fig. 11.

not contaminate the withdrawals, which it would do if injected through the needle in the vein. The saline is used only to keep the blood-way clear and to prevent clotting by stagnation between the withdrawals. The small handle on the valve can be turned in three directions, directing the flow through the needle end into the vein (*7, A*), or open end to wash out any small clot (*7, C*) or allowing of direct suction from the vein (*7, B*, or *5*). For withdrawing the samples the handle is as shown in the ensemble, *4*, *5*, and *6*, and between times it is as seen in *7, A*. In this position the fluid runs slowly through the needle keeping it clear. The blood is withdrawn every 5 minutes and put in a clean test tube. Although the same syringe can be used for all the samples it is better to have 7 clean ones. It is allowed to stand for 10 to 20 minutes after the final estimation and centrifuged. The clear supernatant serum contains the dye and each sample is examined, the amount remaining is determined and the graph is plotted. The estimations are done by comparison with a set of color standards[1] after the serum has been alkalized to bring out the color of the dye.

SUMMARY

This work is not complete. It has all been done on private patients which presents certain difficulties, some of which can be overcome and some can not. Chief of the latter class is the lack of material and follow-up which is necessary to prove certain suppositions. The other and equally important factor is time.

Over 200 tests have been done. Because it seems to be a definite improvement over any tests of liver efficiency now in use, the results would seem to be worthy of further clinical evaluation. The possibilities of its value are great.

CONCLUSIONS

This work must, of course, await confirmation. However if these results are proved to be correct then we can conclude that:

1. We have at our disposal a practical and clinically valuable means of determining liver reserve.
2. This estimation will be of definite value in attempting to lower the mortality in surgical cases—especially gall-bladder surgery—by picking the optimum time for operation.
3. It will be of great value in the prognosis of all surgical cases.
4. The liver is affected in every disease and by every operative procedure.
5. A liver can have its functioning ability or reserve improved if time and the proper measures are taken.
6. Its value in medical cases may be almost as great.

Acknowledgment is made to Drs. W. J. Macdonald, L. H. Werden, and A. D. Konkin for the privilege of using illustrative cases.

This work was made possible through the courtesy of Hynson, Westcott and Dunning who supplied the dye for the study.

NOTE.—Since this paper was submitted for publication, final tests have been performed on the patients illustrated in Figures 6A, 9, 10. They are all normal.

[1]Full directions are contained in the colorimeter which can be obtained from Hynson, Westcott and Dunning, Baltimore. The color standards as prepared are for the 2 mgm. per kilogram dose. When the dose is 5 mgm. per kilogram, the remaining dye is not then a percentage, but rather a number of units. The standard curve is made with the 5 mgm. dose and the 2 mgm. standards. The comparisons are always the same.

PROCTOGRAPHY

Roentgenologic Studies of the Rectum and Sigmoid

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THE roentgenologic examination of rectum and sigmoid is not infrequently interfered with by a number of technical difficulties. First, by reflux of the opaque enema, ileal loops may fill and overshadow the sigmoid and upper rectum; second, too massive a filling before evacuation, or an insufficient one after it, may render the mucosal relief invisible or visible only in part; finally, during the inflow of the opaque medium, the junction of sigmoid and descending colon may form an acute angle which, acting like a valve in interrupting the flow, may cause in the sigmoid such dilatation and elongation as may simulate pathological enlargement (Fig. 1). Although this distention is usually avoided by giving the enema with the patient prone and under continuous rotation, there are instances in which it becomes very difficult to distinguish between true and artificial enlargement, especially in elderly people in whom the elasticity of the intestinal walls is diminished.

Because of its long mesentery and owing to certain phases of physiological activity, the sigmoid normally varies considerably in size and position in the selfsame person. When by mass peristalsis the contents of the transverse colon are driven into the descending portion, the sigmoid fills simultaneously in case the contents are fairly liquid or mass movements very effective; in other instances, when the amount passed on into the descending portion is less, or when the descending colon is especially long, the sigmoid fills after an interval by what appears to be the peristalsis of the descending portion. While being thus filled, the sigmoid relaxes, as previously reported (12), and this physiological enlargement causes the sigmoidal loop to form a wide circle which may reach upward to the epigastrium, and to the right as far as to the cecum (Fig. 2). Then, either immediately, or up to 3 hours before defecation, the sigmoid is evacuated by one or several tonic contractions, whereby it may form, after contraction, a secant of the circle it formed before (12).

The difference in length before and after this movement may be considerable; in one case, the sigmoidal loop was 61 centimeters long before, and 19 centimeters long after contraction, as measured on the films. The barium that is passed on into the rectum distends the latter, whereupon evacuation may occur almost immediately by peristalsis of the rectum. In other cases, there is an interval of from 10 minutes to several hours between the emptying of the sigmoid and that of the rectum. This interval is much increased in dyschesia and in certain anatomical lesions of the distal colon.

From the physiological enlargement just referred to, true anatomical redundancy and

From the Department of Roentgenology, American University of Beirut.

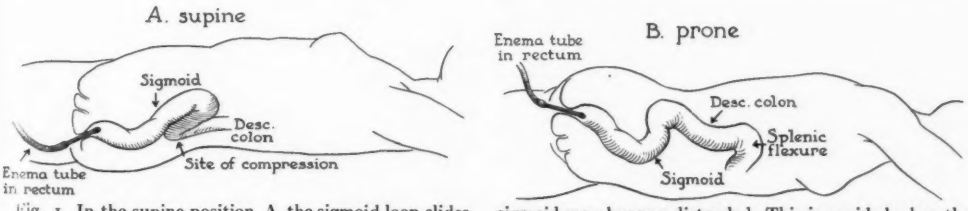
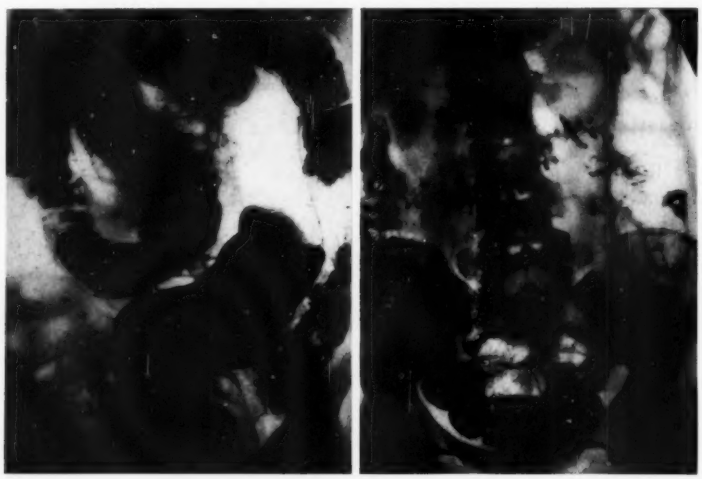


Fig. 1. In the supine position, A, the sigmoid loop slides backward, thus pressing upon the descending colon and obstructing the flow of the opaque enema, whereby the sigmoid may become distended. This is avoided when the patient is placed in the prone position, B.

a b c

Fig. 2. Physiological "enlargement" of sigmoid. a, Colon 25 hours after opaque meal; b, 20 minutes later, mass peristalsis has driven the opaque contents of the transverse colon into the descending portion and sigmoid, the latter being relaxed and enlarged; c, 2 hours later, the sigmoid has again become small by contraction.

megacolon differ by their persistence after evacuation. But even what appears to be a persistent enlargement may, in reality, be the result of functional disorder. For instance, during renal or biliary colic, there may be acute atony of the colon or sigmoid which may cause such enlargement as to simulate true megacolon (11). In other cases, the cause of this atony is not known: in a woman 49 years old who complained of vague discomfort, a shallow ulcer at the posterior wall of the duodenal cap was associated with extreme dilatation and elongation of the entire colon including the sigmoid; but, a



a b

Fig. 3. Pathological atony. a, colon after spontaneous evacuation of an opaque enema. Note the extreme dilatation and elongation; b, 2 weeks later, the colon has regained normal proportions. See text.

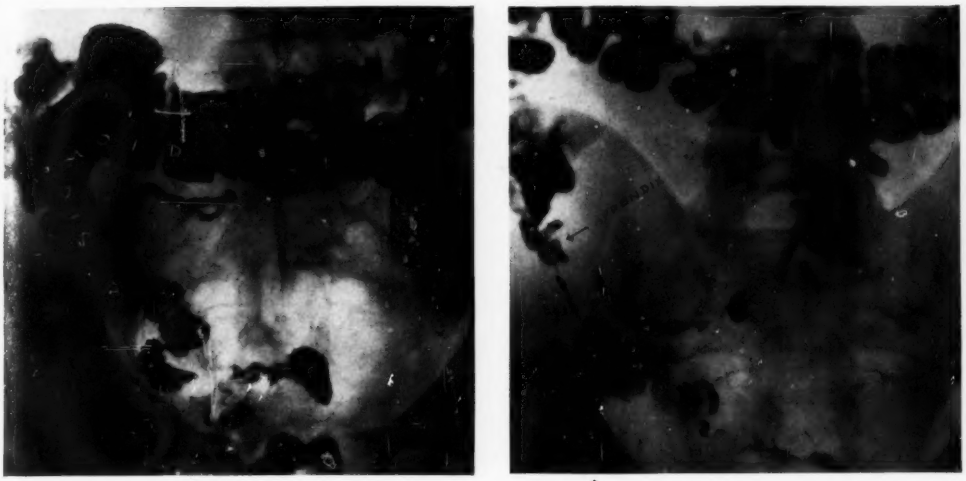


Fig. 4. Roentgenograms in 2 cases of adhesions between sigmoid and cecum which were due to chronic appendicitis. Operative and histological confirmation of the condition was make.

few days later, as well as on three examinations made at intervals during the subsequent 18 months, this enlargement was not seen again (Fig. 3). A similar "pseudo-megacolon" was found by Bernstein in a child during a severe general infection. These observations are concordant with the results of experiments in man (11) and animals (1, 2), which show that paralysis of the colon may be induced by extra-intestinal lesions; they support Alvarez'

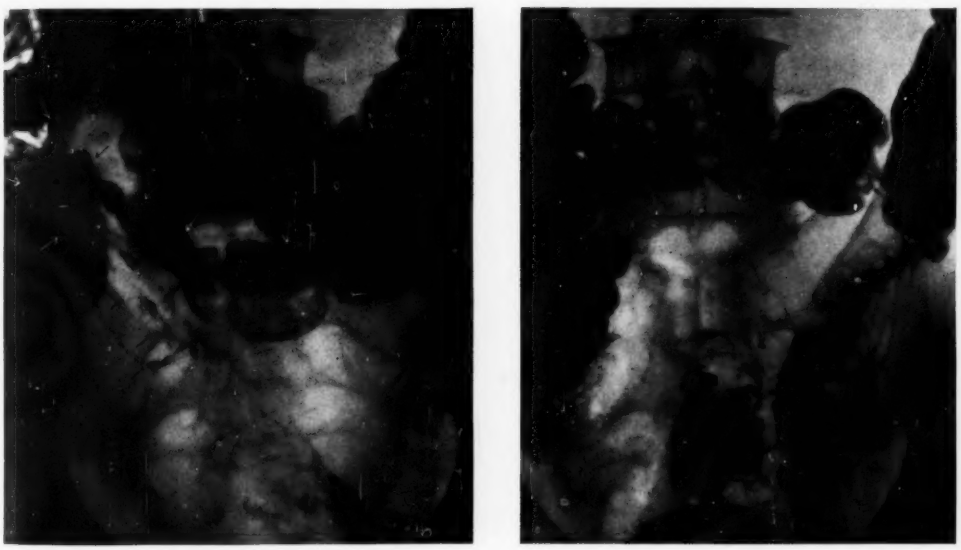


Fig. 5. "Pseudo-adhesion": the angulation and displacement of the sigmoid (arrows) are accidental, as evinced by re-examination, by roentgenogram at right, after 4 days. No adhesions were found on operation.

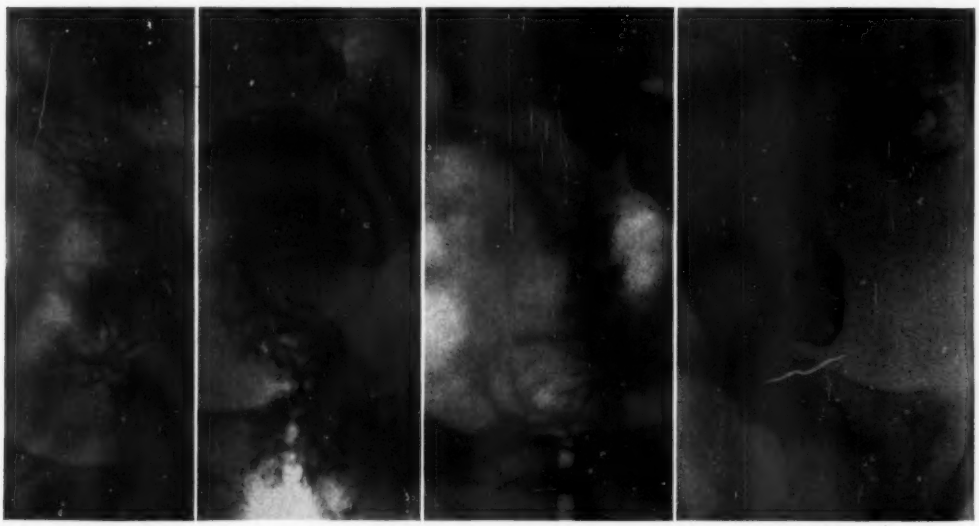
Fig. 6. Sigmoid (arrows) prolapsed into inguinal hernia, *x*.

view that, in these cases, atony is due to inhibitory reflexes, as the intestinal muscle is not damaged (2). The occurrence of intestinal paralysis in renal colic was known to the older clinicians (10).

Displacement of the sigmoid occurs in the presence of adhesions and tumors in the lower abdomen, and in inflammation of the pelvic organs; in the latter condition, deformities and angulations frequently coexist. Displacement to the right results chiefly from perityphlitic adhesions (13); for, owing to the fact that the sigmoid is relaxed for the greater part of the day, it is frequently in contact with the cecum, where it may become adherent when the latter is inflamed (Fig. 4). The top of the sigmoidal loop then may become angulated during contraction at the site of adhesion. Such angulation, however, may be merely temporary and accidental, as illustrated in Figure 5. Hence it is necessary to verify that displacement and deformity are persistent.

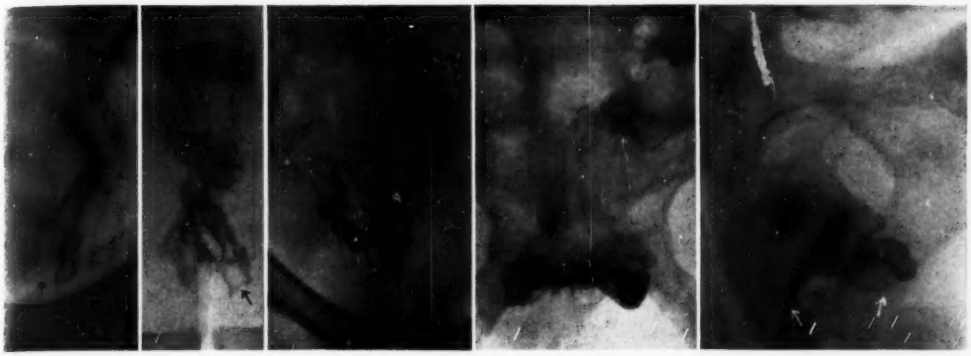
Shortening, narrowing, and rigidity of sigmoid and rectum occur in inflammatory, fibrous, and malignant involvement. Parts of the sigmoid may be found prolapsed into an inguinal hernia (Fig. 6).

As above mentioned, examination of the mucosal relief of rectum and sigmoid is often interfered with by the inconstancy of the filling. Since the interpretation of the mucosal pattern depends entirely and almost exclusively upon a controlled "standard" coating, an attempt was made to provide for constant filling by the following method: The patient is in the prone position; a flexible urethral catheter is introduced into the rectum until the tip of the catheter meets with resistance.



a b c d

Fig. 7. Various types of normal mucosal pattern in rectum and lower sigmoid.



a b c d e

Fig. 8. a, b, Two cases of hepatic cirrhosis with internal hemorrhoids seen in longitudinal, a, and axial projection, b; c, villous proctitis (histological confirmation); d and e, prolapse of rectum around internal sphincter (see text).

By means of a syringe, about 2 cubic centimeters of barium suspension[1] are instilled in order to show the lumen of the catheter on radioscopy. Injection then goes on under radioscopic control until the sigmoid is sufficiently filled, whereupon the catheter is

[1]Any type of barium may be used; we have used the standard mixture given in examinations of the stomach.

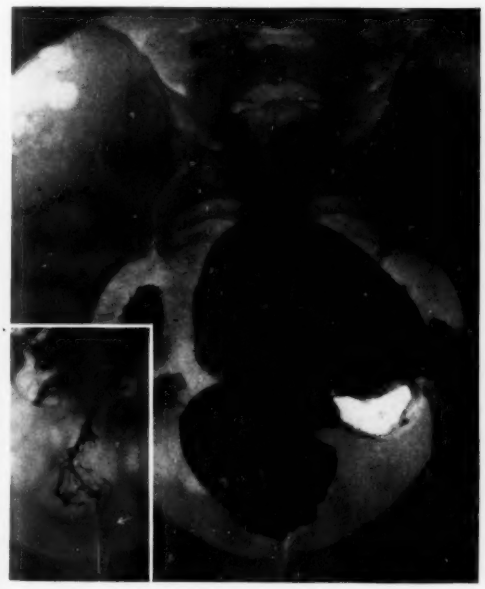
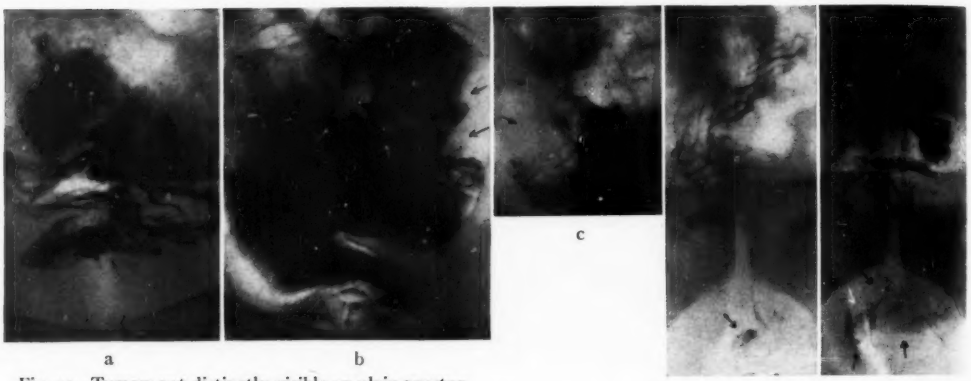


Fig. 9. Dyschezia. Colon 8 hours after barium meal: rectum overfilled, colon almost empty. Barium was retained in the rectum during the subsequent 4 days. Insert: enlargement of internal sphincter (arrow) in the same patient, possibly due to spastic contraction or actual hypertrophy. Compare with normal sphincter (Fig. 7, a; 7, d).

Fig. 10. Volvulus of sigmoid (operative confirmation). Sigmoid loop distended with gas. Mucosal relief of rectum appears as though "cut off."



a b c d e

Fig. 11. Tumors not distinctly visible on plain proctography, but revealed after insufflation of about 15 cubic centimeters of air. a, b, c, Small cancer, circular, of upper rectum (operative and histological confirmation), not visible before air insufflation, a, but revealed after it, b, c; d, e, ulcerating hard tumor within anal canal, not discovered on numerous proctoscopic and x-ray examinations, because both proctoscope and enema tube slipped by the small sinus which led to the tumor; d, before; e, after air insufflation.

gently and gradually withdrawn while injection still continues. As a rule, from 10 to 30 cubic centimeters are necessary to produce the filling desired. If the amount injected seems too large, some opaque fluid is aspirated. After spontaneous evacuation, the entire mucosal relief is uniformly coated. Air insufflation may follow if necessary (Fig. 11).

This method has the following advantages: (1) in the presence of stenosis or inflammation of the rectum, the catheter passes without causing pain, spasms, or such alteration as might change the appearance of the mucosa; (2) the filling is controlled; (3) there is no overshadowing by other loops; (4) no distention is produced that might simulate

Fig. 12. Thrombosed hemorrhoidal vein.

Fig. 13. Intussusception of sigmoid (arrows). Note the overriding of the rugæ. Operative confirmation.

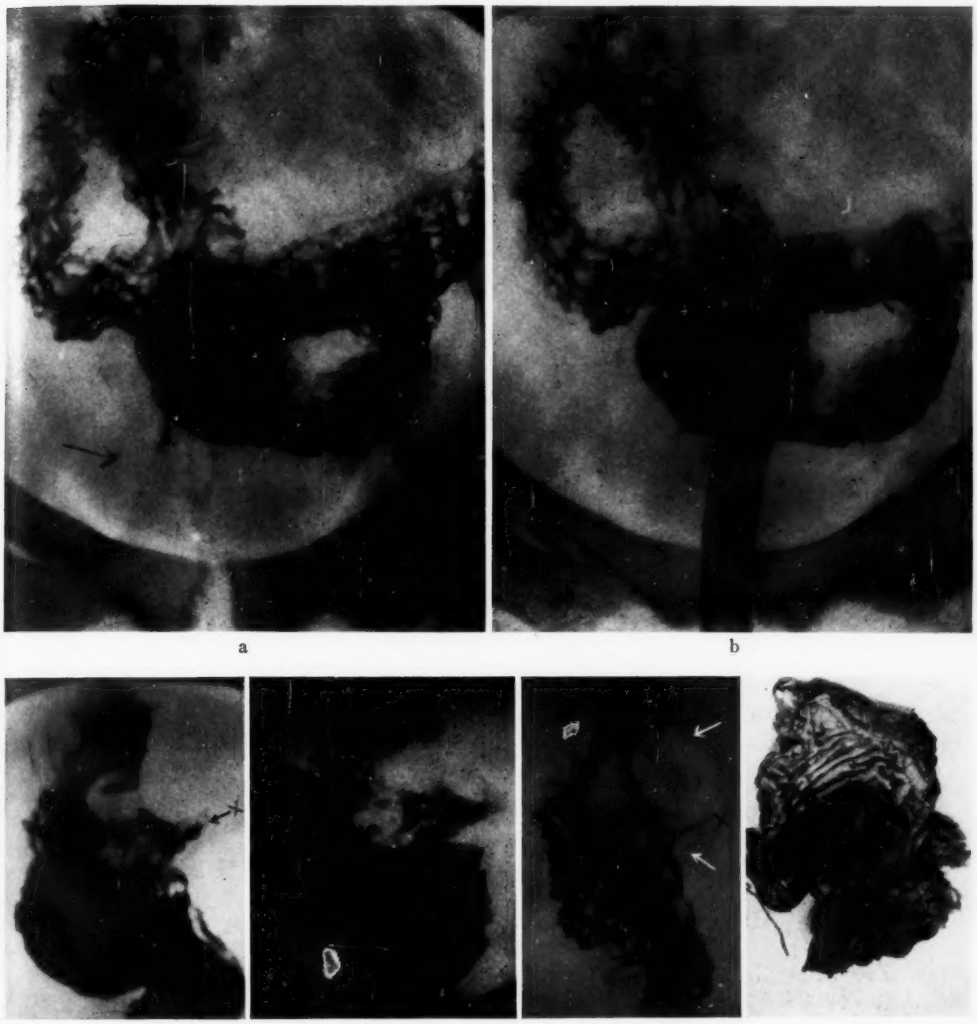
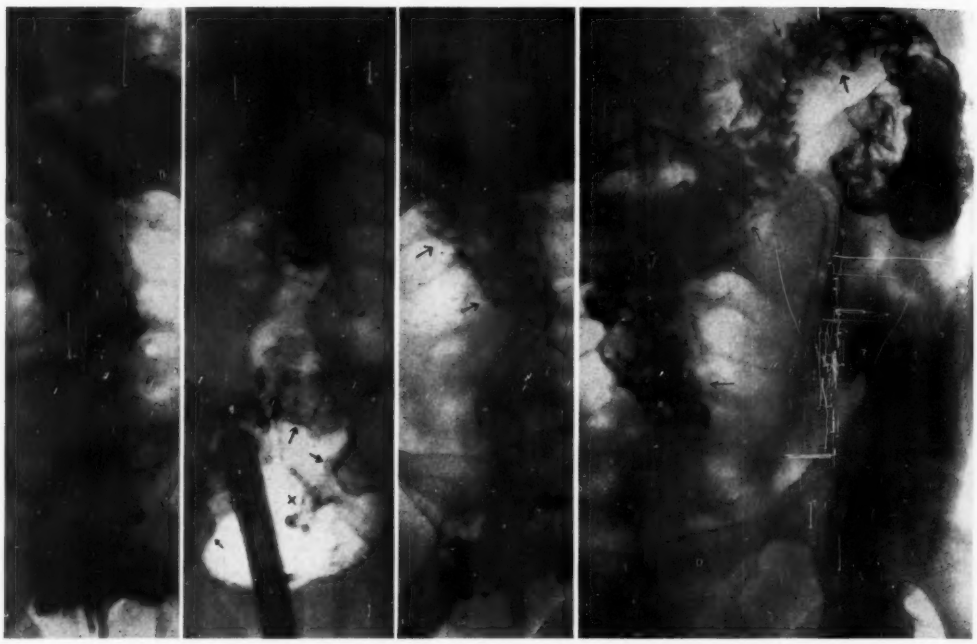


Fig. 14. Cancer of rectum. Opaque enema does not reveal the tumor: the enema tube passes beyond it, b, and after spontaneous evacuation, there is no distinct filling defect, a. Proctography shows tumor (arrows) and its central crater, *x*. f, Specimen from operative removal. Note similarity of roentgenological and anatomical appearance.

redundancy or obstruction. The sole disadvantage of the method lies in the fact that it demonstrates the distal part of the colon only; for completion of the examination, an opaque enema has to be given later by connecting the catheter with an enema device.

Roentgenograms are taken in the oblique position, the patient, supine, being rotated to his left side so that his right iliac crest is raised by about 45 degrees from the Potter-Bucky grid. In this position, the entire length of the sigmoid is shown, and the roentgeno-



a b c d

Fig. 15. Polyposis of rectum (histological confirmation). a, b, opaque enema. a, After evacuation. Rigidity and narrowing definite, polyps partly seen after air insufflation, b; the *x* in b indicates a pedunculated polyp. c, d, Proctography shows the size, number, and position of polyps, and the extent of involvement.

grams thus obtained reveal more details than those taken in the sagittal direction; for in the latter those parts of the sigmoid which turn backward or forward cannot be seen fully (Fig. 16).

In order to prevent irritation, no laxatives and no "cleansing" enemas are given before the examination; one liter of a lukewarm chamomile enema, given either the night before or 3 hours before the examination, is quite sufficient to clear the colon, provided a reasonably soft diet was taken the preceding day.

The main character of the normal mucosal relief in rectum and sigmoid is its wide variability, both individually, and in the selfsame person at different times. While longitudinal rugæ frequently predominate, especially after evacuation, there are normal persons in whom the relief appears fragmented or "feathery" as in duodenum or jejunum. In the rectum, the longitudinal rugæ are commonly interrupted by two transversal extensions, one just proximad to the internal sphincter, the other a few centimeters cephalad to the first (Fig. 7, a). There may be transversal folds at these levels. The upper border of the internal sphincter is marked by a few convergent logitudinal rugæ producing a kind of funnel which somewhat resembles the pattern cephalad of the pylorus (Fig. 7, d). Sometimes the sphincter muscle is recognized by the circular impression it produces (Fig. 7). Proximad to the two recesses mentioned, the mucosa of both sigmoid and rectum is fairly uniform. After spontaneous evacuation, longitudinal folds may prevail in the sigmoid even when the rectum shows a more "feathery" pattern.

In elderly people, the rectum is often seen to prolapse around the internal sphincter; instead of being funnel-shaped, the terminal

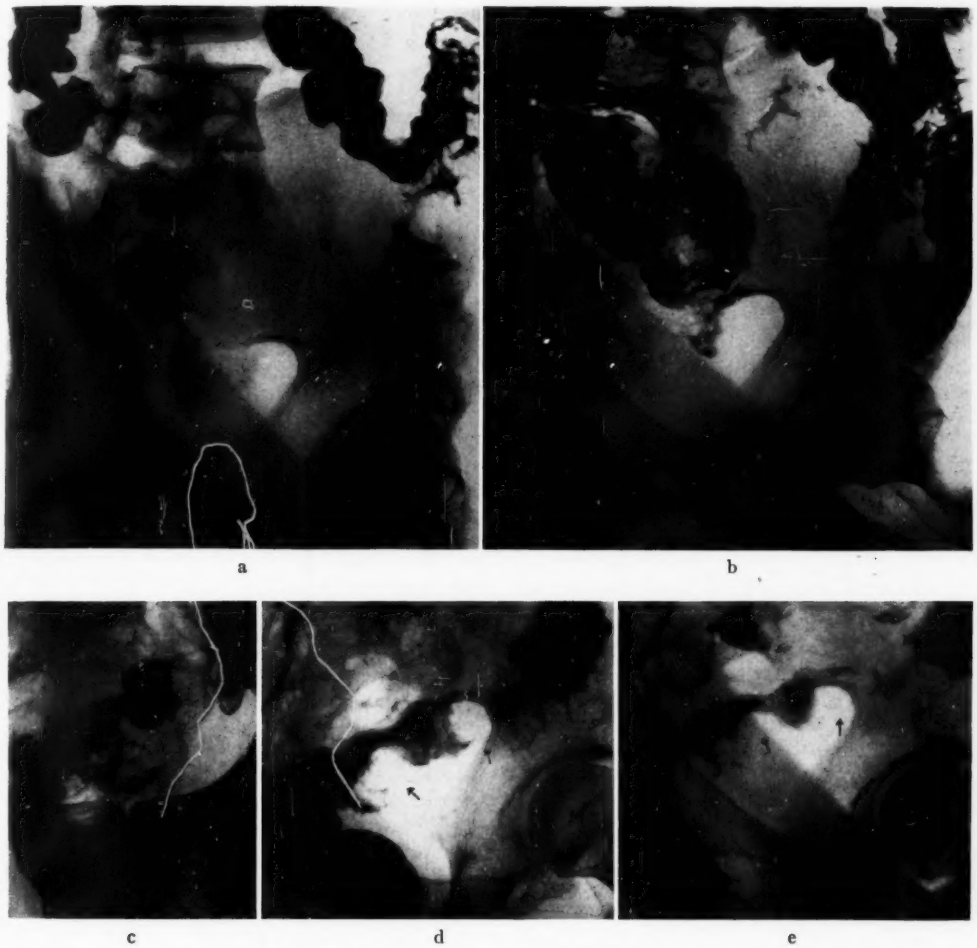


Fig. 16. Cancer of sigmoid (operative and histological confirmation). a, b, opaque enema. With slight filling, a, the tumor is not distinctly visible; with more massive filling, b, reflux into ileum overshadows the diseased region. c, d, e, Proctography in sagittal projection, c, and in oblique views, d, e, with variable amounts of filling.

part of the rectum protrudes in a circular pouch above the anus (Fig. 8, d). Possibly this is a condition which precedes the formation of actual prolapse.

In typical dyschezia, that is, retention confined to the rectum and associated with normal or accelerated passage through colon, the internal anal sphincter has been found enlarged, as shown by increased impression it produced upon the rectal lumen (Fig. 9).

Internal hemorrhoids are not always visible, even in the presence of demonstrable esophageal varices (hepatic cirrhosis). Hemorrhoids cause either rounded defects about 4 to 6 millimeters in diameter, when seen in optical sections; or increased distance between the mucosal furrows, when projected longitudinally (Fig. 8, a). In one case of hemorrhoidal thrombosis, the hardened vessel was seen as a tubular defect (Fig. 12).

a b

Fig. 17. Diagnostic error. Both in oblique, a, and in sagittal projection, b, the lower sigmoid is narrowed in lumen, and there are persistent filling defects in its mucosal relief (arrows). Operation: no tumor; moderate congestion.

Intussusception of the sigmoid has been observed in but one instance; the overriding of the walls is characteristic (Fig. 13).

Volvulus of the sigmoid causes a pathognomonic appearance: at the junction of rectum and sigmoid, the mucosal relief ends abruptly in an oblique line, as though cut through with a razor blade. The distended sigmoid, marked by its gaseous filling, is seen a few inches above this line; obviously, the latter corresponds to the caudad border of the twist (Fig. 10).

Polyps and other tumors are very accurately shown with the technique here described. For example, in a case of a confirmed carcinoma of the rectum in a young woman, the normal enema tube passed beyond the tumor, wherefore the latter escaped visualization (Fig. 14, b). But, in injecting barium through the catheter, the tumor and its central crater were by reflux surrounded with barium, which produced a filling defect visible even before withdrawal of the catheter (Fig. 14, c). In another case, a persistent irregularity of the mucosa of the sigmoid, associated with narrowing of its lumen (Fig. 17) was diagnosed as an infiltrating tumor; but on operation, the region suspected showed merely congestion. The patient, a man 60 years old, had complained of frequent profuse bleeding from the rectum, the cause of which was not elucidated by further clinical and laboratory examinations.

In 2 cases of lymphogranuloma inguinale (or venereum), as verified by positive Frey's tests, the rectum was narrowed, rigid, devoid of mucosal pattern, and pipe-shaped.

Fistulas, diverticula, sinuses, and the like, are easily revealed by any method. Syphilis of the rectum was observed in one patient in whom it produced the x-ray appearances of an infiltrating growth.

In one case of villous proctitis confirmed by biopsy, the rugæ were enlarged and interspersed with polypoid excrescences (Fig. 8, c). In other cases of proctitis, no positive findings were found, as the alterations in the mucosal pattern did not exceed those noted as normal variations.

CONCLUSIONS

By a simple modification of the opaque enema method, roentgen examination of sig-

moid and rectum can be freed of the technical hazards which often impede consistent results. By the procedure here described, the amount of opaque filling in rectum and sigmoid is technically controlled. Both in its advantages and in its limitations, this method resembles the examination of the gastric mucosa: while tumors and similar lesions are demonstrable with a comparatively high degree of accuracy, inflammation often escapes recognition, as individual and physiological modifications of the mucosal pattern are normally more numerous and diverse than the pathological alterations observed, or theoretically expected, in inflammation.

As in the stomach, variations of tone may simulate anatomical alterations. For instance, atony of the sigmoid is physiological during the period at which the sigmoid fills from above; this relaxation frequently amounts to such enlargement as encountered in redundancy and megacolon. A more persistent though also transient form of atony may occur in renal colic and other abdominal diseases as a result of reflex disturbances, and may be produced experimentally by distention of the renal pelvis (11). In statistical investigations on "anomalies" of the colon, these physiological and pathological states of transient atony have hitherto not been taken into account.

SUMMARY

1. A simple technique, proctography, is described by which in roentgen examinations of rectum and sigmoid the opaque filling is technically controlled.

2. With this method, the normal and pathological appearances of rectum and sigmoid, especially of their mucosa, are demonstrable with a degree of accuracy similar to that now attained in roentgen examinations of stomach and duodenum.

3. The mucosal pattern varies normally so much as to render it difficult to recognize typical signs of inflammation, unless there are secondary changes such as fibrosis or well marked mucosal hypertrophy or atrophy.

4. By loss of tone, the sigmoid loop may be greatly enlarged, especially during the physiological relaxation which occurs while the sigmoid fills from above. Besides this normal enlargement, pathological atony, as in renal colic and certain abdominal diseases, may simulate redundancy, megacolon, or obstructive dilatation.

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Fig. 1. Showing the method of hand retraction. The gall bladder has been removed.

Fig. 2. Opening the duct. Note position of sucker and of guy sutures. Inset, Sounds being passed into the duct.

Choledocholithotomy.—Douglas Miller.

CLINICAL SURGERY

FROM ST. VINCENT'S HOSPITAL, SYDNEY

CHOLEDOCHOLITHOTOMY

MacCormick's Technique

DOUGLAS MILLER, F.R.C.S., Sydney, Australia

THE following is a description of the technique employed by Sir Alexander MacCormick, of Sydney, and used by a large number of Australian surgeons whom he trained.

DANGERS AND POSSIBLE COMPLICATIONS

Choledocholithotomy is very frequently performed upon the jaundiced patient, who may therefore be an exceedingly poor operative risk, because of the dangers associated with jaundice and liver failure.

After choledocholithotomy we are faced with the possibility of acute bile duct infection, of bile peritonitis, or of a biliary fistula, the latter resulting from neglect to remove all calculi from the duct. This mistake may not lead to fistula formation unless duct obstruction occurs, but it may lead to that most distressing and humiliating complication, recurrent attacks of pain and jaundice, in no way different from those the operation was designed to cure.

Jaundice undoubtedly constitutes an added operative risk, because of the liability of the patient to hemorrhage. If there is evidence of the jaundice subsiding, or if previous similar attacks suggest that it is likely to subside, I wait for this to occur. However, if there is no sign of the jaundice subsiding, I consider it best to operate with all due precautions, rather than expose the patient to the added risks of prolonged common duct obstruction.

PREPARATION

The general preparation followed is for the patient to be admitted at least 48 hours before operation. A routine aperient is given 24 hours before, and an enema 12 hours before operation. Fluids are encouraged until 4 hours before operation. When jaundice exists the patient is observed for a longer period, the blood coagulation time is estimated and, if prolonged, 10 cubic centimeters of 5 per cent calcium chloride is given intravenously on two consecutive days. If the coagulation time is not thus brought back to normal, a small transfusion of 200 cubic centimeters of citrated blood is given and as a rule this will be successful.

When the patient has been jaundiced for a long time, bile salts administered by mouth for some days and glucose in a readily assimilable form should be freely given. If the patient's condition is grave, 600 cubic centimeters of 5 per cent glucose in saline should be given intravenously on the day before and the day of operation.

Fig. 3. Closure of the duct and the gastrohepatic omentum.

Drawings for Figures 1, 2, and 3 are reproduced through courtesy of *Australian and New Zealand Journal of Surgery.*

TABLE.—LENGTH OF STAY IN HOSPITAL

Case number	Indication for opening duct	Operation	Removal of tube—days	Discharged after operation—days
1	Jaundice	Removal of stone and dilatation	4	24
2	History of jaundice	Dilatation	6	30
3	Jaundice	Removal of stone and dilatation	4	22
4	History of jaundice	Removal of stone and dilatation	3	28
5	Jaundice	Removal and dilatation	4	29
6	Jaundice	Removal and dilatation	3	26
7	History of jaundice	Dilatation	3	22
8	History of jaundice	Dilatation	3	40
9	History of jaundice	Removal and dilatation	3	38
10	History of jaundice	Dilatation	3	20
11	History of jaundice	Removal and dilatation	2	19
12	Jaundice	Removal and dilatation	3	17
13	History of jaundice	Dilatation	2	22
14	Jaundice	Removal and dilatation	2	19
15	History of jaundice	Dilatation	6	22
16	History of jaundice	Removal and dilatation	2	24
17	History of jaundice	Dilatation	5	23
18	Jaundice	Removal and dilatation	3	24
19	Jaundice	Removal and dilatation	3	29
20	Jaundice	Removal and dilatation	3	22

ANESTHETIC

Open ether is the usual anesthetic, though of late cyclopropane reinforced by same basal anesthetic has been much used.

TECHNICAL STEPS IN OPERATION

Position. A small sand bag or "bridge" is placed across the back at the level of the angle of the scapula.

Incision. We are guided by the physical character of the patient. In a patient with a narrow subcostal angle, the right paramedian incision, with lateral displacement of the rectus, is the most generally useful.

In the more common type with a broad subcostal angle, we have come to favor a transverse incision with division of the rectus, or an obliquely placed incision extending from the xiphoid region down and outward, with partial longitudinal splitting and partial transverse division of the rectus. Prior to dividing the rectus muscle I pass a double row of single catgut sutures through the anterior sheath and the muscle in order to control bleeding. The muscle is then divided between these rows.

After division of the rectus in either of the two latter incisions the posterior rectus sheath, including the transversus abdominis muscle, is divided in the same direction.

On opening the peritoneal cavity I make a preliminary exploration and palpate the gall bladder, bile ducts, pancreas, stomach, and duodenum. Three packs are then inserted, one displaces the stomach to the left, one displaces the transverse colon downward, and the third is placed in the right extremity of Morrison's pouch.

It is the usual practice in these operations to do a routine cholecystectomy first, but if the patient's condition is grave, the urgent necessity is to clear the common duct, and the cholecystectomy may be postponed either until the end of the operation, or a subsequent date. If cholecystectomy is performed we do not try exploration of the common duct through the open stump of the cystic duct, as this is usually most unsatisfactory and a waste of time.

The packs already placed are carefully arranged to shut out the peritoneal cavity and the left hand of the assistant is inserted over them with fingers extended exerting a slight traction on the lesser omentum in a caudal and forward direction. No mechanical retractors are used. An excellent view of the right free border of the gastrohepatic omentum is now obtained. A long strip of gauze

is packed down into the foramen of Winslow, and fills the space to the right of the foramen. The nozzle of a sucker is held close to the duct in the right hand of the second assistant. The peritoneum over the duct is incised longitudinally, and two "guy sutures" of fine silk are inserted on each side of the duct at some point convenient for incision.

With a fine pointed scalpel, the duct is now opened by an incision 1.5 centimeters long in the line of the duct. The bile which escapes is evacuated in the sucker. The identification and opening of the duct may present some difficulty in cases in which there has been much inflammatory thickening or adhesion formation. Needless to say such difficulties call for punctilious care in identification of the duct before any incision is made. An exploratory puncture with a fine needle will readily clear up any confusion between bile duct and portal vein. When the duct is open stones may be removed with a malleable scoop or Desjardin forceps. This is not always a simple matter and frequently a stone will need to be gently dislodged and milked up to the opening by the surgeon's fingers, manipulating the duct from its anterior and posterior aspects in the foramen of Winslow.

Stones impacted in the lower end of the duct may present extreme difficulty particularly as they are frequently so difficult to feel. When the surgeon has dislodged all obvious calculi, a fine probe or sound is inserted into the duct and gently guided until it finds its way into the duodenum. This is followed up by a slightly bigger Lister sound and this in turn by others gradually increasing up to about 10 to 13. As each sound reaches the sphincter of Oddi, it pauses momentarily and then with a slight jerk slips into the duodenum. The sensation is similar in a very delicate way to the sensation of a uterine dilator slipping through the cervix. During this maneuver it is no uncommon experience to find that on increasing the size of the sound, an obstruction is encountered, though the previous ones slipped most readily into the duodenum. This obstruction is always a stone, and fresh effort must be directed to its removal. It is common to find that once again a slightly larger sound will meet with another obstructing stone. Such experiences as this shed light on those cases in which jaundice follows on operations in which the surgeon has been content merely to establish the patency of the duct with a probe.

When the ampulla of the duct has been sufficiently dilated, a scoop should be passed up to explore the hepatic duct. The common bile duct is then sutured with fine interrupted catgut, and the split peritoneum sutured over it with a continuous catgut suture, which is carried up to peritonealize the gall-bladder bed when cholecystectomy has been performed. A large tube at least 1.5 centimeters in diameter is inserted through a stab incision low in the loin, and placed with its end lying just to the right of the common bile duct. A narrow ribbon wick threaded through the tube will serve to anchor it in position. The packs having been removed, the abdomen is closed. We suture each aponeurotic layer with interrupted mattress sutures of chromic gut. Interrupted silkworm gut and continuous catgut coapt the skin. A separate dressing seals the main wound from the stab wound. Gauze is then packed around the projecting end of the tube so that drainage fluid will be absorbed.

POSTOPERATIVE CARE

The tube usually drains a little bile for 2 or 3 days, but sometimes the closure of the duct is so satisfactory that no drainage occurs. The wick is withdrawn at the end of 24 hours, and the tube is withdrawn when drainage has ceased. During the first 24 hours the patient is best nursed in a semirecumbent position with a slight tilt to the right.

A long experience with this technique has proved its great value. Adequate common duct drainage is established into the duodenum. Patients rapidly lose their jaundice, and it is most unusual for external drainage to last longer than a few days.

The average convalescence is little if any longer than that of cholecystectomy, and postoperative troubles are minimized.

In a series of 20 consecutive cases in which patients were treated in this way at St. Vincent's Hospital there was no mortality and the length of stay in hospital in each case is shown in the accompanying table.

AN OPERATION FOR THE REPAIR OF DIRECT INGUINAL HERNIA

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A BRIEF résumé of the problems associated with the repair of direct inguinal hernias was reported in a previous publication. It is the purpose of this communication to describe an operative technique, an essential part of which was devised by Dr. C. W. M. Poynter, dean of the University of Nebraska School of Medicine, and used by him in 1908 in the treatment of one case. This case, twice recurrent following previous repairs, has remained cured. Because Dr. Poynter subsequently diverted his talents to an academic career, the operation was given no further trial until its recent application in 6 cases by the author. The operation appears to have such obvious merits that it is reported without recommendation from a large and extended clinical trial. It utilizes a flap of the pectineus portion of the pelvic fascia and the pectineus fascia and muscle to obturate the defect in the floor of the inguinal canal. This flap is sutured to the transversalis fascia and to the deep surface of the internal oblique aponeurosis, so that in reality a small segment of the pelvic wall is shifted mesialward where it forms a deep or first line of defense. This support is supplemented by obliteration or reinforcement of the inguinal canal by one of two methods, in both of which living sutures of fascia are used.

TECHNIQUE

Omitting a description of the routine details of exposure of the inguinal canal, elevation of the cord from the canal, and the inversion or excision of the sac, the transversalis fascia and peritoneum are separated from loose attachments below Poupart's ligament and retracted mesialward, exposing those portions of the pelvic fascia and of the pectineus muscle and fascia which cover the superior ramus of the pubis. This exposure extends from the pubic spine to the superior border of the femoral canal. The femoral vessels are retracted superiorly and laterally. Gimbernat's ligament is incised to expose the pectineus fascia down to the pubic spine. This fascia and the

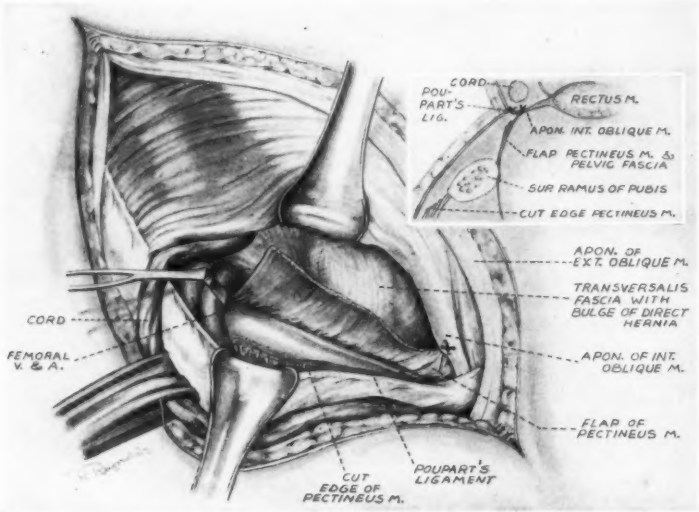

Fig. 1. A pedicled flap of pectineus muscle and fascia and pelvic fascia has been raised from the superior ramus of the pubis and the first and lowermost stitch approximating it to the aponeurosis of the internal oblique has been placed. The insert illustrates the repair as seen in cross section.

underlying muscle fibers are then incised along the anterolateral margin of the pubic ramus from the pubic spine to the upper limit of the exposure. A pedicled flap, including both fascia and muscle, is raised from the anterior and mesial surfaces of the ramus, and this flap is of sufficient length to reach the deep surface of the internal oblique aponeurosis and conjoined tendon without tension. The flap retains its normal deep attachment throughout its breadth so that suture of its free margin to the mesial border of the inguinal triangle forms under this triangle a strong supportive wall which is continuous with the pelvic living membranes. The free margin is approximated with interrupted sutures of silk or chromic catgut to the deep surface of the free border of the conjoined tendon, internal oblique aponeurosis, or rectus sheath as presented by the anatomical relations in the individual case.

A second line of defense is then created by approximating Poupart's ligament to the internal oblique aponeurosis and conjoined tendon behind the cord, if this can be accomplished without tension. A pedicled strip of external oblique fascia is used as a continuous suture to bind these tissues and additional support is given by interrupted sutures of silk. This part of the repair was described in a previous publication[1] and is illustrated in Figure 2.

If, however, Poupart's ligament cannot be approximated to the tissues forming the mesial border of the inguinal triangle without tension, the space is bridged by weaving strips of fascia lata across it by the technique described by Gallie.

It is important, regardless of the type of technique used, to include the triangular fascia in the lowermost suture to seal the area immediately above the pubic spine (Fig. 2.) The superficial fascia is approximated over the cord and the skin closed with interrupted inverted mattress sutures.

[1] Bisgard, J. Dewey. Surg., Gynec. & Obst., 1939, 68: 113.

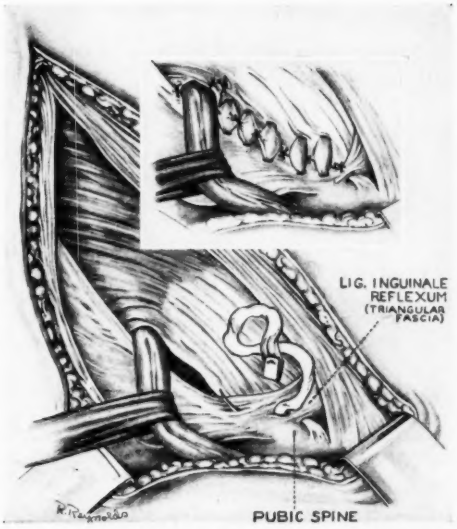

Fig. 2. A second layer of support is added by approximating the borders of the inguinal triangle and binding them with a pedicled strip of external oblique fascia used as a continuous suture. If the borders cannot be approximated without tension, strips of fascia lata are weaved between them after the technique of Gallie.

CONCLUSION

An operative technique for repair of direct inguinal hernia is reported. The operation appears to have certain mechanical merits.

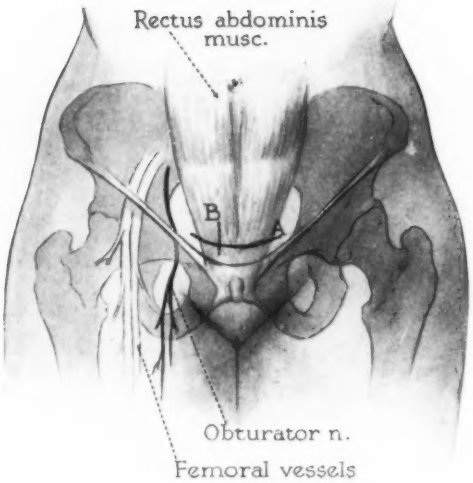

Fig. 1. *A*, Skin incision (Pfannenstiel) for exposure of the obturator nerve. *B*, Incision of the anterior sheath of the right rectus abdominis muscle.

Fig. 3. Blunt extraperitoneal dissection with index finger along the posterior surface of the horizontal ramus of the pubis until the obturator nerve is palpated.

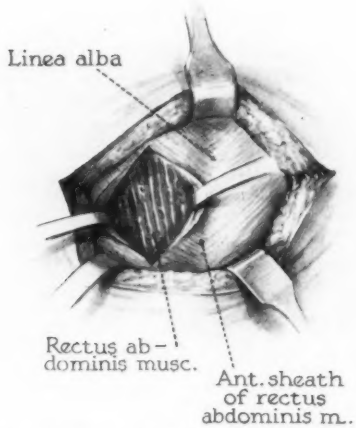

Fig. 2. Exposure of the lateral margin of the right rectus abdominis muscle.

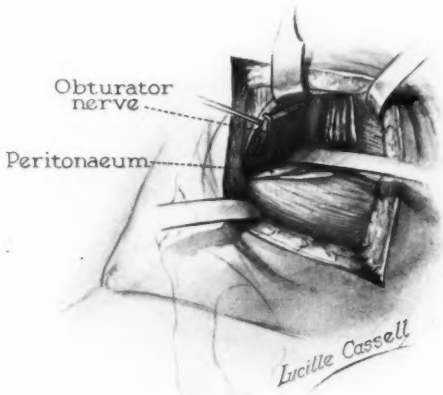

Fig. 4. Oblique view with peritoneum retracted medially to expose the right obturator nerve.

Intrapelvic Extraperitoneal Resection of the Obturator Nerve.—Fremont A. Chandler and Ferdinand Seidler.

INTRAPELVIC EXTRAPERITONEAL RESECTION OF THE OBTURATOR NERVE

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IN severe spastic paraplegia or hemiplegia, overactivity of the adductor muscles of the thigh is undoubtedly the greatest obstacle to useful functioning of the lower extremities. A "scissors" gait or position of the legs not only impedes progression but contributes to the development of deformities of the knee, ankle, and foot. The correction of the disabling overactivity of the adductor muscle groups by active and passive stretching with or without retention in plaster, or by tenotomy or myotomy of the adductor groups, has been extensively employed but with rather disappointing results. However, in cases presenting structural shortening of the adductor muscles, these procedures may be necessary.

The conversion of the rigid spastic state into that of a flaccid paralysis by neurectomy has been found to be most beneficial. In 1910, Stoffel studied the topography of the obturator nerve and in 1911 described an operation in which the branches of the obturator nerve were resected in the upper inner thigh. This has a number of disadvantages, namely, difficulty in keeping the wound clean, the possibility of a tender scar in this region, as well as the difficulty of locating both the anterior and posterior branches (sometimes 3 branches) of the nerve. In 1914, Selig gave an anatomical description of a proposed operation of intrapelvic extraperitoneal resection of the obturator nerve performed through a lateral abdominal incision. In 1921, Loeffler and Gocht resected the nerve by the extraperitoneal route, both by a partial resection of the insertion of the rectus abdominis muscle, the former using a midline incision and the latter a Pfannenstiel incision. Their results were satisfactory. Bonnet, in 1932, resected the obturator nerve near its origin through a lateral abdominal incision locating the nerve upon the psoas muscle. In 1930, Wischnewsky presented a new operation in which he exposed the nerve through a vertical incision between the inner and middle thirds of the Poupart's ligament. The pectineal fascia was cut and the pectineus muscle released and retracted laterally exposing the fascia of the obturator externus. This fascia was incised and the branches of the obturator nerve were exposed and resected. In 1936, Klimov described a partial resection of the obturator branches as well as the branch communicating with the saphenous nerve in cases of ulcer or gangrene of the leg. He exposed the nerve through a vertical incision on the upper inner thigh.

We have employed intrapelvic extraperitoneal resection of the obturator nerve in 84 instances at the Children's Memorial Hospital. The results have been so uniformly satisfactory that we are prompted to present the technique of the operation that we have evolved.

OPERATIVE TECHNIQUE

In bilateral resection of the main trunk of the obturator nerve, a transverse (Pfannenstiel) incision is made through the skin and subcutaneous tissue of the lower abdomen following the normal transverse crease just above the pubis (Fig. 1*A*). The anterior fascia of the rectus abdominis muscle is exposed by blunt dissection. The anterior fascia or sheath of the rectus muscle is then split vertically over the center of its distal portion (Fig. 1*B*). The lateral portion of the rectus sheath is elevated and retracted laterally exposing the lateral margin of the muscle (Fig. 2). The rectus abdominis muscle is retracted medially and the fascia transversalis and the peritoneum exposed. The index finger is used as a blunt dissector following the posterior surface of the muscle to its insertion in the body and the horizontal ramus of the pubis, entering the space of Retzius which is filled with loose, fatty, areolar tissue (Fig. 3). The finger is then gently directed laterally and more deeply along the horizontal ramus of the pubis displacing the bladder and the lateral folds of the peritoneum posteriorly until the upper portion of the obturator fascia overlying the obturator internus muscle is palpated. The obturator nerve is then located as a small cord-like structure on the inner pelvic wall just below the lower margin of the horizontal ramus of the pubic bone. One inch ribbon retractors are inserted extraperitoneally to hold the peritoneum and bladder medially. The fatty areolar tissue overlying the obturator nerve is opened with a forceps and the nerve exposed. The nerve may

be identified by stimulation and by its course as it enters the neural canal of the obturator fascia. The nerve is then separated from adjacent blood vessels and is elevated with a small blunt hook (Fig. 4). A ligature is placed at each of 2 levels to prevent bleeding and the intervening portion of the nerve is excised. Care must be taken not to tear any of the small veins of this area, and the possibility of anomalous arteries must be kept in mind. After inspection of the wound for bleeding points, the retractors are removed and the peritoneum permitted to fall back into place. The opposite side is exposed in a similar manner. The fasciæ, subcutaneous tissues, and skin are sutured and a compression dressing applied. No cast is used. In unilateral cases a vertical lower rectus incision is preferred.

In our series, no complications have arisen. The relaxation of the adductor groups by this method has been more satisfactory than by other operations which we have employed.

The advantages of the operative technique described above may be summarized, in part, as follows: (1) The main trunk of the obturator nerve is exposed satisfactorily with a minimal amount of trauma. (2) The incision is in a location least exposed to contamination and is also inconspicuous. (3) The incision of the fascia is supported by the rectus muscle reducing the possibility of hernias. (4) The retention of the legs in an abducted position by braces or casts is not necessary. (5) The active use of other muscle groups of the leg is not even temporarily impeded. (6) A satisfactory correction of adductor spasm is obtained.

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AN INSTRUMENT TO MEASURE ARTERIAL PULSATION IN THE DIGITS

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IN an effort to determine the condition of the circulation in the fingers and toes, an instrument has been constructed which measures arterial pulsations in the digits. It is an extremely sensitive, differential manometer constructed on the same principle as the Pachon oscillometer. With it the magnitude of pulsations in the digits may be recorded under varying conditions of health and disease.

The instrument (Fig. 1) was constructed for us by Mr. William Hurst, instrument maker at the Duke University instrument shop. It consists of an air-tight chamber, *A*, within which is a small cup-like chamber, *B*, covered by a thin rubber diaphragm on which rests a small aluminum upright which, through a system of gears, operates a recording pointer. With the valve, *C*, open, pressure may be built up in a small cuff applied to a digit to any desired level, the pressure in chambers *A* and *B* being equalized. With the valve then closed, pressure variations caused by the digital pulse are recorded from oscillations of the pointer. The instrument is quite stable and is not affected by ordinary building or room vibrations. It has a sensitivity of 0.002 centimeter of mercury per millimeter scale division as compared to a sensitivity of 0.012 centimeter of mercury per millimeter scale in the Boulitte oscillometer used to record pulsations in the arms and legs. It is capable of responding to impulses at the rate of 15 per second.

The instrument is portable; its operation is extremely simple and easy, requiring no technical skill; and it may be used with extremities in a water bath at various temperatures. In these respects, it adapts itself better to clinical use than the sensitive digital plethysmographs which have been devised by Johnson and by Turner.

Digital pulses have been found to vary with the constantly changing vasomotor reactions in each individual. Yet, with control of the environmental temperature by placing the extremity in a water bath at various temperatures, abstinence from smoking for at least 2 hours, and with the subject relaxed and composed at normal body temperature, readings are believed to give a sufficiently reliable index of the efficiency of circulation in the digits for practical clinical use. The pneumatic cuff must be applied to the base of the finger in each case. And to eliminate the effect of reactive hyperemia following occlusion, the cuff is not left in place longer than a minute and readings are not repeated oftener than every 10 minutes.

To determine the effect of environmental temperature on the digital pulse, readings have been made on a series of normal adults with the arm and hand in a water bath at various temperatures. With the subject seated comfortably, an arm and hand are immersed in an arm tub at 45 degrees C. After 10 minutes, the cuff is applied to the index finger and inflated to 160 millimeters of mercury. Readings are made at this pressure and at 140, 120, 100, 80, 60, 40, and 20 millimeters of mercury. Temperature of the water in the arm tub is then dropped and after 10 minutes at each temperature, readings also made at 40, 35, 30, 25, and 20 degrees C. Chart 1 shows a typical curve obtained in this way. It will be seen that maximum pulsation occurs at about the diastolic pressure and t the higher temperature. As the temperature is dropped, the magnitude of pulsations changes little until the temperature of the bath is at 30 degrees C. when a significant re-

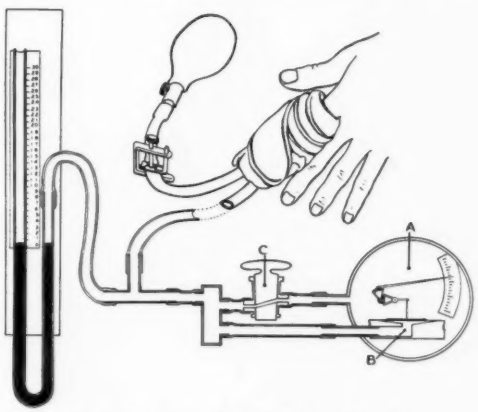

Fig. 1. Diagram of the digital oscillometer.

From the Department of Surgery, Duke University School of Medicine.

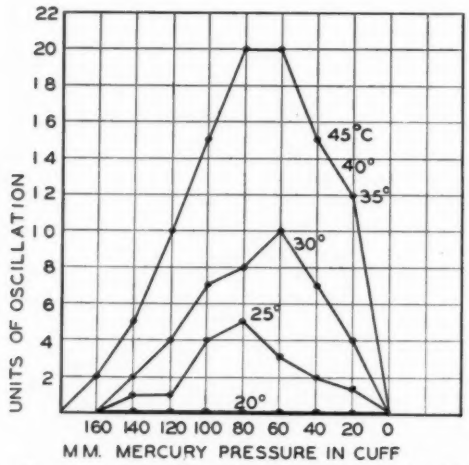

Chart 1. Chart of the digital oscillations of the right index finger, normal adult, aged 20 years, with the arm and hand in a water bath at various temperatures. The blood pressure was 120/75. Pulsations were first charted at 45 degrees C. and then at decreasing increments of 5 degrees C. each to 20 degrees C. At 30 degrees C. pulsations were significantly reduced, and at 20 degrees C. they were absent, indicating extreme vasoconstriction at this temperature.

duction occurs. At 20 degrees C. pulsations have either disappeared or are so feeble as to register only a fraction of a millimeter deflection of the needle.

Variations from this normal range of pulsations in the digits, we believe, will give valuable information in the recognition of obliterative or of vasospastic conditions in the digital vessels. Thus an obliterative process in the arteries may be expected if at full vasodilatation with the ex-

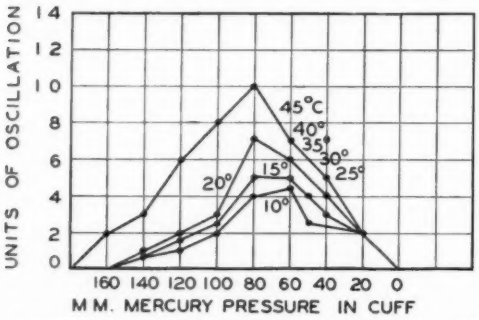

Chart 3. Chart of the digital oscillations of the left great toe 10 days after left splanchnic and left lumbar sympathectomy. Good pulsations remain after the environmental temperature has been dropped to 10 degrees C.

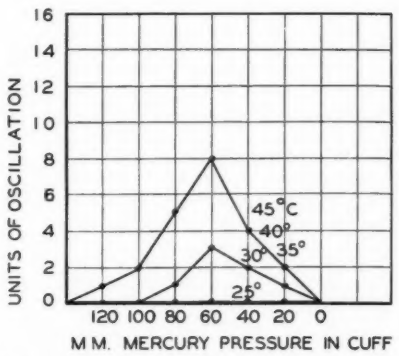

Chart 2. Chart of the digital oscillations in the right index finger of a man, aged 54 years, with sclerodactylia and Raynaud's syndrome. At the higher temperatures, pulsations never reached the normal level. As the temperature was reduced, pulsations disappeared at 25 degrees C., indicating a tendency to vasospasm at a higher environmental temperature than normal.

tremity in a warm bath the magnitude of pulsation fails to approximate a normal level. While, with a normal range of pulsation at full vasodilatation, disappearance of pulsations at temperatures higher than 20 degrees C. would indicate the presence of a pure vasospastic condition.

Chart 2 shows the pulsations in the index finger of a man, age 54, with sclerodactylia and Raynaud's syndrome. Pulsations did not rise to a normal level on immersing the arm in a warm bath. This might be interpreted as being caused either by an obliterative process within the artery or because the inelastic and contracted integument of the finger failed to allow full pulsation. The fact that pulsations disappeared at a higher temperature than normal would indicate an in-

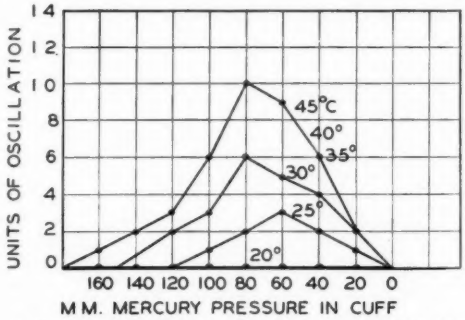

Chart 4. Chart of the digital oscillation of the right great toe of the same patient as in Chart 3. No sympathectomy has been done on this side. Pulsations were entirely obliterated at 20 degrees C.

creased sensitivity to cold, with vasospasm at a higher environmental temperature than normal.

Pulsations exactly similar to those in Chart 2 were observed in another patient, a male, aged 25 years, with typical Raynaud's syndrome but without sclerodactylia. The pulse at the wrist was normal as were oscillometric readings in the forearm and arm. The maximum digital oscillation at 45 degrees C. was 7 millimeters and all pulsations had disappeared when the temperature of the arm tub was dropped to 25 degrees C. These readings would seem to indicate the presence of both an obliterative and a vasospastic element in the digital vessels such as is seen in the advanced stages of Raynaud's disease in which the digital arteries are narrowed by thickening of their intimal coats and are incapable of full expansion.

In most of the obliterative arterial diseases observed in the vascular disease clinic, pulsations in the major vessels at the wrist or ankle of the affected extremities cannot be felt, and no digital pulsations can be recorded. One patient, a male, aged 45 years, with Buerger's disease and a gangrenous toe, had palpable radial pulses at each wrist and maximum pulsations in the forearm as recorded with the Boulitte modification of the Pachon oscillometer of 2 units on the left and 1½ on the right. Digital pulsations could not be obtained at any temperature on the right and were only faintly seen on the left at full vasodilatation. In a man of 66 years with arteriosclerotic gangrene of the right great toe, pulsations could be felt in the left posterior tibial and dorsalis pedis artery and maximum pulsations with the oscillometer on the left thigh were 9, and above the left ankle, 2½. No pulsation could be detected in the left great toe at any temperature, indicating an advanced degree of obliteration of the digital arteries.

The effect of sympathectomy on the digital pulse in the great toe with foot and ankle in a water bath at various temperatures is shown in Chart 3 as compared to pulsations in the unsympathectomized toe (Chart 4) of the same individual. The patient was a male, aged 20 years, in whom left splanchnic nerve resection and resection of first and second left lumbar sympathetic ganglia had been performed 10 days previously for Hirschsprung's disease. At room temperature, the left great toe showed a maximum oscillation of 10 millimeters while that in the right great toe was 4 millimeters. As shown in the charts, the sympathectomized toe continued to show good pulsations in a bath at 10 degrees C. which was as low a temperature as the patient could comfortably stand, while in the toe not operated upon, the pulsations were feeble at 25 degrees C. and had completely disappeared at 20 degrees C.

SUMMARY AND CONCLUSIONS

An instrument is presented which measures the magnitude of pulsations in the fingers and toes. Measurement of these pulsations at various environmental temperatures, it is believed, will give valuable assistance in the recognition of peripheral vascular diseases and in the differentiation of vasospastic from obliterative processes in the digital arteries.

In the preparation of the instrument described, we wish to acknowledge with appreciation the valuable assistance of Dr. J. E. Morgan, physicist to the Duke Hospital.

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A NEW OPERATION FOR METATARSALGIA AND SPLAY-FOOT

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THE kind of foot in which the operation to be described is indicated is one which exhibits the signs of marked relaxation of the structures which hold the metatarsal region together. It has been called the "splay-foot" or "spreizfuss." In this clinic we call it the metatarsalgic or accordion foot.

It is to be found in the main in women in third and fourth decades. It is based probably upon foot weakness in childhood. In adult life the holding together of the metatarsal region is accomplished in a manner by narrow shoes, but further development of the relaxation is determined by the higher heel of feminine shoe apparel which throws an abnormal strain upon the anterior arch. Symptoms of metatarsalgia then make their appearance, of which the Morton's toe and the feeling of "walking on the bones" are classical examples.

From the Department of Orthopædic Surgery, Bellevue Hospital and the New York University College of Medicine.

Presented at the November, 1937, meeting of the Orthopædic Section of New York Academy of Medicine and Philadelphia Orthopædic Club.

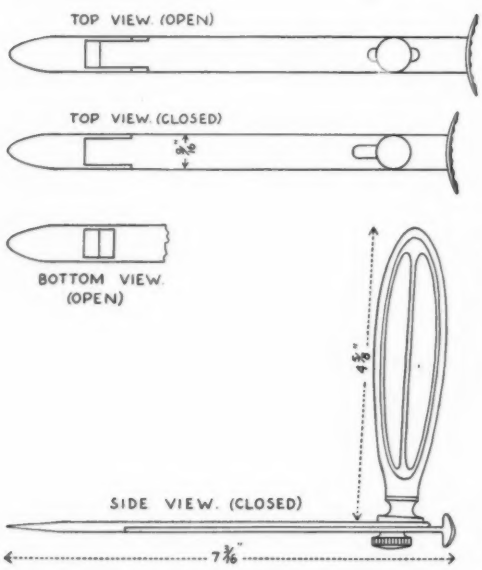

Fig. 1. The fascial introducer.

In time the narrow shoe is no longer adequate to hold the foot together because the first metatarsal head (and frequently the fifth), resent the pressure, and respond by the development of more or less of a bunion. In the meantime a greater or lesser degree of hallux valgus has developed. In this stage the woman patient has a closet full of shoes with none of which she is entirely happy. This is entirely understandable because a shoe is no longer adequate.

The treatment which has heretofore been utilized in this type of foot is: (1) support of the metatarsal arch by a suitable device; (2) wider shoes with a lower heel; (3) intensive development of the intrinsic foot musculature by exercises; (4) some type of operation for the hallux valgus, usually for the relief of the pressure symptoms of the extruded first and fifth metatarsal heads.

In some occidental urban communities it seems to be still possible to induce women in the age period mentioned to adopt a wide shoe with a low heel for habitual use. In my community I have found this to be largely unfeasible, and when accomplished, a rather thankless enterprise. As to the possibilities of the development of the intrinsic foot musculature, such attempts are apt to be conducted in a half-hearted fashion, and at best are vitiated by the inevitable return to the esthetically prized shoe as a means of personal adornment.

The encircling fascial band operation is advanced as a practicable means of holding such a foot together in a permanent way. It offers the assurance that recurrences following the usual operation for hallux valgus will not take place, that hallux valgus may be prevented, and that no artificial support of the metatarsal arch will be necessary.

In the last 20 months about 30 feet have been operated upon by this method with satisfactory outcome.

INSTRUMENT FOR PASSING FASCIAL BAND AND TECHNIQUE

The instrument that has been devised looks a good deal like the old Sluder tonsillotome. Its extremity is somewhat pointed and beveled so that it may be passed with a minimum of resistance through the soft tissues. The slot is about ¼ inch in width and is equipped with fine

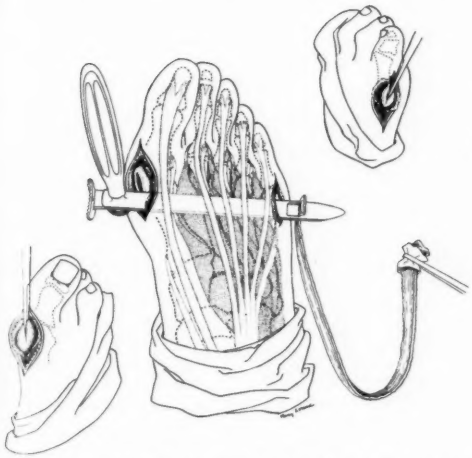

Fig. 2. Encircling the metatarsus with a flat fascial band. Curved incisions are made about the first and fifth metatarsal heads. Dorsal view.

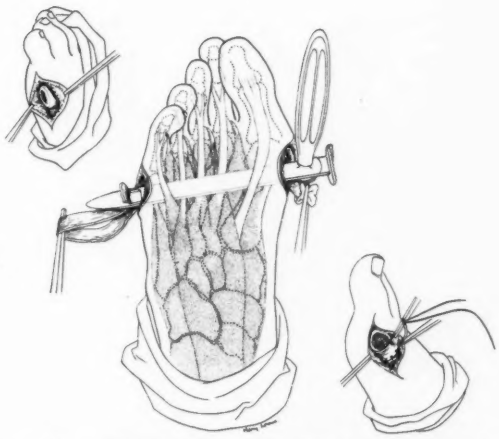

Fig. 3. The course of the band on the plantar aspect. The method of securing the ends of the band has been modified to include a fascial knot as indicated in the text.

teeth upon which the gliding top portion of the instrument impinges upon the fascia, thus holding it firmly.

The curved incisions are made about the first and fifth metatarsal heads with their convexity dorsally. The prominent extruded portions of the first and fifth metatarsal heads are excised with a chisel, and the sharp remaining edges are smoothed off. An incision is made in the thigh and a 5/8-inch wide strip of fascia lata about 8 inches in length is removed. The special instrument is introduced through the incision over the first metatarsal head and is passed across the forefoot deeply to all the extensor tendons and emerges through the incision over the fifth metatarsal head. The aperture of the instrument is opened and one end of the fascia is fixed in it and the instrument is drawn back carrying the fascia with it as a flat band. The instrument is passed across the foot on the plantar aspect and here the instrument passes deeply to the flexors of the great toe, then superficially to the flexors of the second, third, and fourth toes, and again deeply to the flexor tendon of the fifth toe. The other end of the fascia is placed in the aperture and drawn across the foot through the inner incision. The forefoot is compressed by an assistant. The two ends of the fascia are split for a short distance into a wide portion and a narrow strip. A knot is tied with these narrow strips. The wide portion is overlapped and secured with several fine silk sutures. The level at which the fascial band is passed is just proximal to the metatarsal heads. The incisions are closed and covered with dressings. The foot is wrapped in several layers of sheet wadding, the great toe being wrapped separately. A firm flannel bandage is wound over this sheet wadding to maintain compression of the forefoot and to maintain the great toe in a moderately corrected position. This dressing is renewed after 5 days. At the end of 12 days the sutures are removed and the compression of the forefoot is maintained for 3 weeks longer by an encircling adhesive plaster dressing. Weight bearing is allowed after 3 weeks. No metatarsal support is used.

A NEW OPERATIVE PROCEDURE FOR REPAIR OF RUPTURED CRUCIATE LIGAMENTS OF THE KNEE JOINT

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IN view of the numerous articles written on injury to the cruciate ligaments of the knee joint, no attempt will be made herein to discuss the causative or pathological factors or the diagnosis of the condition. But, to my knowledge, the plastic procedures described herein for repair of this complication have not been presented previously.

For repair of the anterior cruciate ligament, the knee joint is exposed through a lateral parapatellar incision, which allows inspection of the joint and preparation of the medial femoral condyle for reception of the reconstructed ligament. A second incision is made over the tendons of the medial hamstring group of muscles, the semitendinosus tendon is identified and severed at its musculotendinous junction. The belly of the muscle is then sutured to the semimembranosus muscle. The semitendinosus tendon is freed up to its point of attachment on the tibia. Through a hole made with a three-sixteenth inch drill in the anterior aspect of the tibia, emerging at the origin of the anterior cruciate ligament, the tendon is passed through into the joint. Next, a hole is made through the lateral femoral condyle posteriorly, emerging from the posterior aspect of the inner condylar notch. The tendon is then drawn through and sutured to the periosteum. The knee is held in full extension while the tendon is being sutured (Fig. 1).

For repair of the posterior cruciate ligament of the knee, a median parapatellar incision is used. The joint is inspected and the medial femoral condyle is prepared for reception of the new ligament. For repair of the posterior cruciate ligament the drill hole through the medial femoral condyle is placed well forward, and an incision similar to the one previously described is used for obtaining the semitendinosus tendon. By blunt dissection the posteromedian aspect of the popliteal space is exposed. For accurate placing of the drill hole in the tibia, the hole in this instance to be drilled backward and outward from a position proximal to the site of insertion of the semitendinosus tendon, a Kirchner wire is used. When a Kirchner wire is used as a guide, with exposure of the popliteal space, the procedure is carried out under direct vision and an accurate location is obtained. The tunnel in the tibia is

From the Section on Orthopedic Surgery, The Mayo Clinic.

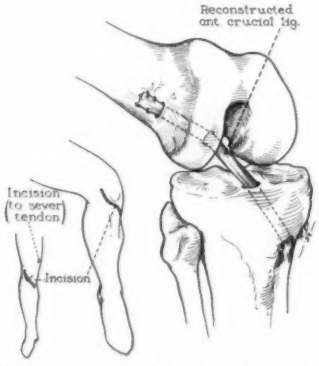

Fig. 1. Technique for repair of ruptured anterior cruciate ligament. Illustrating the lateral parapatellar incision for inspection of the joint and preparation of the medial femoral condyle for reception of the reconstructed anterior cruciate ligament, the incision over the medial hamstring group of muscles to sever the semitendinosus tendon, and the holes (3/16 inch) extending through the anterior aspect of the tibia and the posterior portion of the lateral femoral condyle, through which the reconstructed anterior cruciate ligament is to be passed.

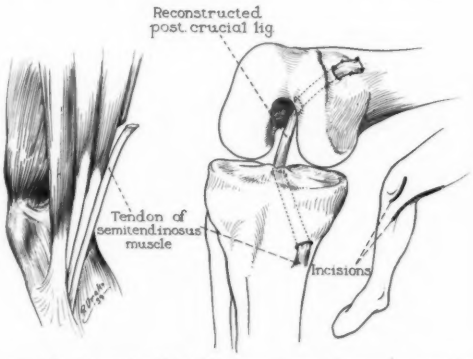

Fig. 2. Technique for repair of ruptured posterior cruciate ligament. Illustrating the median parapatellar incision, the incision for obtaining the semitendinosus tendon, and the drill holes (3/16 inch) through the medial femoral condyle and the tibia, and the correct flexion of the knee for suturing.

prepared by passing a three-sixteenth inch drill over the wire. The tendon is then passed into the popliteal space. Through the anterior incision made in the knee joint, a hole is punched through the capsule posteriorly and the tendon is pulled into the joint and passed through the medial femoral condyle. In suturing the tendon it is well to hold the knee in moderate flexion (Fig. 2).

After the repair of both the anterior and posterior cruciate ligaments of the knee is accomplished, a plaster-of-Paris leg cast is applied and is worn by the patient for about 4 weeks. On removal of the cast, physical therapy and active exercises are instituted. At the end of about 8 weeks full activity of the leg usually can be permitted. To hasten infiltration of the transplanted tendon with callus and to promote incorporation of the tendinous tissues into the bone, it is well to scarify the portions in the bony structure. This new procedure offers a normal anatomical reconstruction of the ligaments accomplished by a method which presents few technical difficulties.

PALLIATIVE COLOCOLOSTOMY FOR INOPERABLE MALIGNANT LESIONS OF THE COLON

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Rochester, Minnesota

ALTHOUGH the percentage of operable cases of malignant lesions of the colon has increased a great deal in the past two decades, there remains a large group of cases in which removal of the growth is technically impossible. In this group, prevention of death due to obstruction of the bowel is the only end one can hope to accomplish by surgical measures. This can be achieved by making a permanent external colonic stoma. However, if relief of obstruction can be obtained by use of a method which does not leave a stoma in the abdominal wall and which does not entail prohibitive operative risk, that method would seem preferable.

We have reviewed the small series of cases in which palliative colocolostomy has been performed at The Mayo Clinic. In all these cases the growth was too extensive for any type of resection to be at all feasible and in a large number of cases generalized abdominal carcinomatosis was present. In all, 42 patients were subjected to the procedure which is under consideration, 6 of whom died after operation, an operative mortality of 14 per cent; this apparently is not prohibitive in view of the marked debility and generally poor operative risk presented by patients of this group. Of the operative deaths, 5 were from peritonitis and 1 was from pulmonary embolism.

Table I shows, as would be expected, that lesions of the splenic flexure comprised the largest subgroup in this series, undoubtedly because of the anatomical inaccessibility of the part; also, the operative mortality was higher in this group.

It is interesting to note (Table II) that all deaths occurred among those patients in whom the sigmoid colon was used in the anastomosis and that in all but one of these instances the anastomosis was made between the transverse colon and the sigmoid colon. To draw conclusions from such a small series is dangerous but the fact just brought out suggests that undue tension on the anastomosis increases the operative risk. Another factor to be considered is that in many cases in which the sigmoid was used for the anastomosis, the omentum was not long enough to protect the line of suture.

In all but 3 of the cases, the carcinoma was primary in the colon. Of the patients represented in these cases, one had a primary carcinoma of the stomach with obstruction of the transverse colon; 1, carcinoma of the tail of the pancreas with obstruction of the splenic flexure of the colon; and 1 a carcinoma of the left kidney with extension to, and obstruction of, the splenic flexure.

Of the 36 patients who survived operation, the average duration of life after operation was 11.5 months. In the case of carcinoma of the kidney mentioned, the patient survived 52 months after operation. Thus, these patients were given an average of almost a year of fairly comfortable existence without an external colonic stoma.

Of the patients who survived operation, the average stay in hospital was 18.5 days and in 15 cases the period was less than 15 days. In all but 4 cases, closure was made without drainage.

From the Division of Surgery, The Mayo Clinic and The Mayo Foundation.

TABLE I.—SITUATION OF LESION AND OPERATIVE MORTALITY

Site of involvement	Cases	Deaths	Mortality (per cent)
Transverse colon	9	0	0
Splenic flexure	16	4	25
Descending colon	5	0	0
Sigmoid	12	2	16.6

TABLE II.—PORTIONS OF THE COLON USED IN THE ANASTOMOSIS AND OPERATIVE MORTALITY

Portions of colon used	Cases	Deaths	Mortality (per cent)
Ascending-transverse	1	0	0
Ascending-sigmoid	1	0	0
Transverse-transverse	3	0	0
Transverse-descending	13	0	0
Transverse-sigmoid	14	5	35.7
Descending-descending	1	0	0
Descending-sigmoid	6	1	16.6
Sigmoid-sigmoid	2	0	0
Not recorded	1	0	0
Total	42	6	14.2

A SIMPLE METHOD FOR KEEPING DRY BLADDER FISTULAS FROM CERVIX CANCER

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WHEN carcinoma of the cervix ulcerates into the floor of the bladder, a very disagreeable and uncomfortable condition ensues. To the infected necrotic cervix discharges is added the pooling of stagnant urine in the vagina, thus making this tender mucosa increasingly irritated, inflamed, and sore.

The care of this condition has been unsatisfactory. Transplantation of the ureters into the sigmoid has been considered, but at this stage of the disease the ureters are usually dilated from the stricture caused by cancer extension into the broad ligament, and the prognosis for length of life is too uncertain (2 to 6 months) to make this extensive operation practicable. Bilateral lumbar ureterostomy has been done occasionally with success.

The employment of a permanent urethral catheter will keep some patients dry if the hole in the bladder is high up near the cervix and is not too large. Very often the catheter soon irritates the urethra, however, and the patient demands its removal. Locally, we have tried to keep these patients comfortable by means of rubber sheet and double pads placed underneath the hips and thighs, and by giving them a supply of perineal pads which they may change as frequently as necessary (every 20 to 40 minutes). Some have used a sea sponge in the vagina. Others have used an inflated toy balloon.

Urologists have, during the past few years, made increasing use of continuous suction to carry off the urine from draining bladder wounds (5). The principles of applying suction to an open wound or orifice are that no vacuum be formed in the wound, and that there be no cupping action on the walls or bottom (3).

Various devices have been described to fit on to the body surface comfortably in order to dispense with drainage tubes or for use when these tubes are not needed (1, 2, 4, 7). In all such devices a gauze wick lies in the urine or in the secretion to be absorbed. Air is sucked through a perforated catheter, tube, or mask attached to the gauze. The suction pulls the urine through the gauze, into the tubing, and then into a trap bottle.[1]

The slightest suction or cupping pull in the vagina is painful, but a piece of gauze can be inserted into the vagina, attached to a perforated catheter outside the vaginal orifice, and the proper suction will transport the urine out into a bottle and keep the vagina clean. We have used the Hendrickson catheter attached to the Stedman electric suprapubic pump. This catheter ends in a flat spade-like tube, on one surface of which are 6 to 8 large perforations. A thick gauze wick is attached to this tube, and the free end is

[1] Dr. William L. Sherman called our attention to these devices.

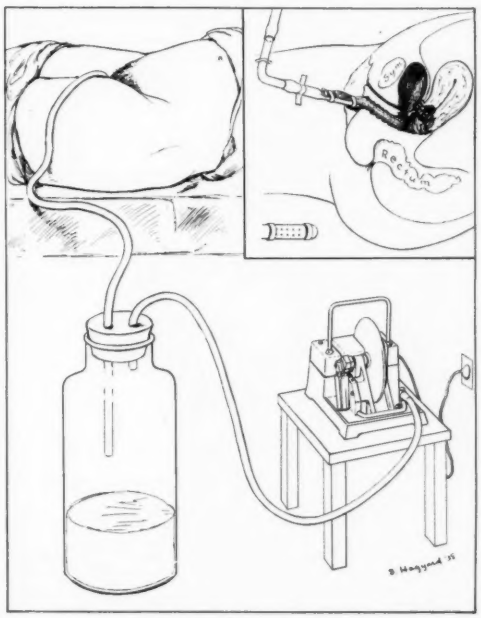

Fig. 1. Suction drainage applied to vagina for urinary fistula. Tubing from catheter is lead into a trap bottle to which mild suction is applied by means of a Stedman electric suprapubic pump. Insert in upper right shows gauze wick in vagina. The outer end of the gauze is held against the perforations in the end of the catheter. The catheter is taped on to the inner thigh and does not enter the vagina.

From Mercy Hall Tumor Clinic and Hospital.

moistened and inserted 3 to 4 inches into the vagina. The catheter remains just outside the vagina. The tubing is then lead over the patient's thigh to a 1 gallon drain bottle on the floor. The pump is attached to the other tube of the bottle (Fig. 1).

The vaginal wick must be changed as it becomes soiled, that is, every 1 or 2 days. No other care is necessary except the routine cleansing of tubing and bottle (6).[1]

[1]Though we have not had an opportunity to try it, we feel that a similar device will keep an intestinal fistula dry if the drainage is liquid and thin.

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THE SURGICAL TREATMENT OF INFILTRATING CARCINOMA OF THE BLADDER

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THIS paper will discuss briefly the best treatment for infiltrating carcinoma of the bladder. By best treatment I mean the treatment that gives the best end-results. This treatment will naturally vary with the stage of the disease when the patient applies for treatment.

In those cases in which the tumor and involved bladder wall can be excised, this type of operative treatment, often involving a re-implantation of the ureter, gives the best results. In some of the more extensive growths total cystectomy, if feasible, gives surprisingly good results as judged by the criterion of 5 year cures. In other more or less extensive growths the introduction of radon seeds through a cystotomy or through a cystoscope may have to be employed for one reason or another, such as the patient's poor general condition, poor kidney function, etc. This is always a hit or miss affair, as one cannot accurately delimit the extent of the infiltration process by sight or by palpation from within the bladder. Despite these handicaps, a small percentage of patients so treated seem to be definitely cured. The end-results, however, are far inferior to those obtained in resectable cases. In addition to the group mentioned, there is an unfortunate series of neglected patients on whom no surgery is feasible, and in these we have to attempt to control the disease with deep roentgen therapy using the Coutard technique. As yet, even at the Curie Institute, no cures have been accomplished with this therapy. Our cases have all been dismal failures; our hopes for this type of therapy in benign and malignant cases have not been realized, and according to the publications of Lacassagne (Curie Institute) his experience has been much the same as ours.

The various publications of more or less enthusiastic propagandists have confused members of the surgical profession as to the proper methods of approach to the question of the treatment to be applied in any particular case of tumor of the urinary bladder. That group of tumors, which are definitely malignant and which invade the bladder wall or the projecting mass on the bladder wall, present therapeutic problems which are capable of being met only by the experienced surgeon, who is able to avail himself of the various surgical procedures as they are indicated. For those surgeons who see tumors of the bladder only occasionally, in view of the confusion in the literature, it becomes difficult to decide what to do. Many years ago to assist in the decision as to the proper therapeutic approach, the American Urological Association Registry was established to classify the results of the various efforts in therapy and to formulate a clearer understanding of what the proper therapy should be.

Those of us who have had an extensive series of cases (in our clinic we have treated almost 700 patients) have gradually come to a better understanding of the problem involved, and it is most encouraging to see that the last report of the Registry in 1936 confirms the conclusions that we have reached, namely, that surgical excision and resection gives the best end-results.

Further confusion, in addition to that caused by the above type of propagandist, has been caused by the attempt of some few pathologists to group these tumors into 4 classes, calling the benign papillomas "Group 1 Carcinoma."[1] Fortunately Major R. O. Dart, who is acting as our registrar, has decided that this type of grading is not valid, accurate, or reliable, and recognizes only 3 types of epithelial bladder growths, as I have insisted for years. He says: "For all practical purposes epithelial tumors of the bladder may be classified as (a) papillary, (b) papillary and infiltrating, and (c) infiltrating. Carcinoma of the bladder cannot be graded on the basis of cell differentiation alone. The most practical method of grading is based on a combination of physical findings and histopathological examination."

In our experience we have found, in agreement with the above, that there are on the one hand benign papillomas and on the other 2 types of carcinoma: (1 A) papillary carcinoma with atypism

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Dr. Beer passed away August 13, 1938.

[1]Surgeons under the influence of this type of pathological interpretation have repeatedly sent me patients and slides diagnosed incorrectly as carcinoma, when transcystoscopic therapy might have been applied in the patients' homes without the patients traveling hundreds or thousands of miles for the application of the proper therapy.

of cells plus invasion of the stroma and occasional lymph vessel thrombi; (1 B) papillary tumors with the above characteristics plus an infiltration and invasion of the bladder wall to varying depths; and (2) more or less solid, more or less nodular, infiltrating carcinoma running well into the bladder wall and occasionally extending widely in a horizontal direction.

An analysis of the results published by the Registry based on approximately 1,400 cases of tumor of the bladder, shows that in the treatment of infiltrating carcinoma the results by surgical therapy are infinitely better than by any other method. This is our experience, as published in 1927 at the International Congress, Brussels, and later (1935) in my monograph (1), in which our cases were again studied. It is evident from the Registry's report that implantation of radon seeds through cystotomy wounds has given only 8.8 per cent of 5 year cures, whereas surgical, partial cystectomy has produced 18.5 per cent of 5 year cures. From this it must be evident that those who rely entirely upon the use of radium are not giving the patients with infiltrating carcinoma of the bladder the care they deserve.

An analysis recently published (2) on total cystectomy in this disease shows that the more radical the surgery, the higher the percentage of 5 year cures. In a series of 24 malignant tumors of the bladder in which a total cystectomy had been performed, 6 patients died following the operation. Of the patients operated upon up to 5 years ago, there were 11 cases, with 2 operative deaths. The 9 patients surviving the operation showed a 55 per cent survival for 5 years and over. These results with total cystectomy in the most extensive bladder tumors point in the direction which we have indicated, i.e., that radical excision, with or without re-implantation of the involved ureter, obtains without a doubt the very best results. The 5 year cures in partial resection are less than after total cystectomy, probably because we were unable to make as complete a removal of all the microscopic deposits of cancer cells in the former instance. In 88 cases of carcinoma of the bladder, papillary and infiltrating, we had an operative mortality of 15 cases. Sixty-five patients could be followed to test the value of this therapy and 24 patients were cured for 5 years, which is twice as high as that reported in the Registry cases, but as we have stated this is considerably less than are curable by total cystectomy. The results with the total cystectomy operation point the way for us, and demonstrate conclusively to me that the more radical the operation in these infiltrating growths, the better our results. For smaller infiltrating carcinomas we cannot as yet substitute total cystectomy and we must still adhere to partial cystectomy, making wide resections so as to encompass the whole of the diseased area.

In closing let me again emphasize the importance of learning the technique of partial cystectomy with or without ureteral reimplantation as well as the technique of total cystectomy with implantation of the ureters in the skin or in the bowel, as all other methods of approaching this most difficult problem are hit or miss affairs and do not give the patient a square deal.

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EDITORIALS

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JULY, 1939

THE QUESTION—ULCER OR CARCINOMA?

GRANTING that under medical treatment many patients with uncomplicated gastric ulcer are relieved of their symptoms and that there is a disappearance of roentgenological evidence of the ulcer, it is likewise well known that certain gastric ulcers complicated in one way or another do not respond satisfactorily to medical management. This is particularly true of an ulcer situated on the posterior gastric wall and which through protective perforation has invaded the pancreas. It is not the gastric ulcer, complicated by perforation, continued bleeding or recurrent massive hemorrhage, or persistent gastric retention in which much difference of opinion exists as to what the management shall be. Practically all internists and surgeons with particular interest in gastric lesions recognize these complications as more or less distinct indications for surgical intervention. It is the crater lesions with none of these complications in which there is lack of unanimity of opinion as to what the appropriate treatment shall be. In many of these cases the question arises—what is the true nature of the lesion—benign ulcer or carcinoma?

The relationship of carcinoma to gastric ulcer is a matter which requires due consideration in many gastric lesions. The importance of this relationship lies not so conspicuously in the question of the frequency with which malignant degeneration in a benign gastric ulcer occurs. Sufficient evidence is at hand to indicate that such a change may and does occur often enough to be reckoned with in certain cases in which chronicity has been established and response to medical management has not been complete. A more absorbing problem in the ulcer-carcinoma relationship is that of the difficulty not infrequently encountered in differentiating a benign ulcer from a carcinomatous ulcer or an early ulcerating carcinoma. In many instances the clinical, roentgenological, and gastroscopic findings in a gastric lesion leave considerable doubt as to just what the true nature of the lesion may be. Every surgeon of experience with gastric lesions has on occasion, with the abdomen open and with the lesion in his hand, felt uncertain as to whether it was a benign one or neoplastic. The benignancy or malignancy of the lesion can often be determined only by the competent pathologist.

The size and location of the lesion as depicted roentgenologically are of importance in differentiating the benign ulcer from the malignant lesion. While lesions with a crater of less than 2.5 centimeters in diameter are not all benign, and not all lesions of a greater diameter are malignant, nevertheless, the probability of malignancy in the latter lesions increases

proportionately to an increase in the diameter of the crater. Lesions of the greater curvature and of the anterior gastric wall are nearly always malignant. In lesions so situated few if any liberties are allowable so far as observation and medical management are concerned.

Appropriate to this discussion and pertinent to the problem of diagnosis, the therapeutic test merits due consideration. As an aid in differentiating a benign ulcer from a malignant lesion it is not always a reliable one. Temporary clinical improvement has often been noted following dietary and other forms of medical management of ulcer when instituted in a patient harboring a gastric carcinoma, and roentgenological and gastroscopic studies at repeated short intervals are subject to error in interpretation even by competent observers in these respective fields. The value of the test as a differential aid is dependent upon the selection of cases for its employment and upon the competency of interpretation of the observations at frequent intervals. It has been the experience of every gastric surgeon upon surgical exploration of patients in whom a medical regimen has been continued following faulty interpretation of the original therapeutic test to find inoperable carcinoma. The value of the test as an aid in the differential diagnosis of certain gastric lesions has been definitely established, but adherence to the fundamental principles which includes adequate interim treatment, careful observation and competent interpretation, is necessary for reliance.

Lack of improvement in the clinical and roentgenological manifestations following careful medical treatment and competent observation over a period of several weeks not only suggests that the lesion is not responding, but also justifies uncertainty regarding the true nature of the lesion. Surgical intervention must be considered in cases in which such uncertainty exists, and the urgency for surgical treatment is great when the evidence predominates in favor of a malignant lesion.

Unquestionably the ulcer-carcinoma problem bears a direct relationship to the operability and curability of gastric carcinoma. Strange as it may seem, the operability and curability of carcinoma of the stomach in general and by and large has shown little if any increase during the past 25 years. Today clinical inoperability is manifested in at least 50 per cent of the patients who harbor a malignant lesion of the stomach; and in at least half of those patients, in whom by clinical and roentgenological studies operability seems probable, surgical exploration discloses wide extension of the disease in the stomach or to extragastric structures, precluding partial or total gastrectomy. In the remainder of the cases gastric resection is possible either as an operation curative in purpose or to provide palliation. Few surgeons have the opportunity through early recognition of the disease to perform gastric resection in 20 per cent of the people who harbor carcinoma of the stomach.

The gastric lesion is a medico-roentgenologic-surgical problem. Whatever the many factors may be which contribute to the present status of the operability of malignant lesions of the stomach, the physician and internist occupy strategic positions in their relationships with patients. Only through evoking the aid of the competent roentgenologist may the physician most conclusively differentiate the functional from the organic gastric disturbance. Only through careful interpretation of clinical and roentgenological evidence and through early surgical intervention in all cases in which doubt exists as to the true nature of the lesion may the doubt be obviated and the curability of gastric carcinoma enhanced.

VERNE C. HUNT.

EMBOLECTOMY FOR PERIPHERAL EMBOLISM

THE operative treatment of emboli in major peripheral vessels was developed by Einar Key into a useful standard treatment for suitable cases before 1920. Especially following his address before the American College of Surgeons in 1924 the operation began to be used successfully in this country by a number of surgeons. By the early 1930's many surgeons in this country and Scandinavia and a few in England and on the Continent had had sufficient experience with the operation to save a very large proportion of the limbs operated upon. If done early, under eight to twelve hours, the circulation should be completely re-established in 50 to 75 per cent of the cases. The technique is not difficult for one trained in the use of fine silk (as many are today) and, from the patient's standpoint, it is a very easy operation. However, in 1933, wide publicity was given the use of alternating suction and pressure in the treatment of all forms of peripheral arterial occlusion and many patients were treated with a machine who might have had the embolus removed. No doubt patients with peripheral emboli have been saved from threatened gangrene following such treatment. However, no series of cases to date has been presented in such form that the results can be compared to the several series of surgical results that have been published. Even if acute gangrene is avoided by such treatment it is not unlikely that many cases have permanently impaired arterial circulation. Another medical treatment has also been recently suggested and used in many cases with results that are quite possibly not much better than the results of no treatment at all. I refer to the use of antispasmodics such as papaverine. If those who advocated its use had ever seen an artery at operation for embolism with its diameter reduced fully one-half by the spasm that takes place below the obstruction, they would not be sanguine about the good results of any drug that could safely be given. There is also, as well pointed out in the recent article by Griffiths,[1] the danger that an antispasmodic, if it is efficacious in promoting the downward movement of an embolus, might move it from a less dangerous to a more dangerous bifurcation.

Enough time has elapsed for definite proof of the efficiency of such medical treatments to be brought forth if such proof were available. Lacking it, it is high time that all surgeons return to embolectomy as the primary treatment of early cases of embolism located from the aorta to the popliteal space. Pressure and antispasmodic treatment may be given after operation if indicated. But embolectomy, because of the time factor, is never indicated if medical treatment is failing or has failed.

If patients are seen late, the indications are entirely different. Although Leriche advocates arterectomy as useful, it may well be that the "pressure boot" is the best treatment. Certainly embolectomy is not indicated. In these cases, however, one must keep in mind that long continued rest and protection from too much heat or cold are all important in the cases without gangrene. Early amputation as soon as a reasonable degree of demarkation has taken place is the only treatment for those with gangrene.

CHARLES C. LUND.

[1]Griffiths, D. L. Arterial embolism. Lancet, 1938, 235: 1339-44; see also editorial, Ibid., p. 1365.

MEMOIRS

CHARLES H. MAYO

IN the death of Dr. Charles H. Mayo the surgical profession has suffered a grievous and irreparable loss. He was one of its outstanding leaders, a great surgeon who undoubtedly made more important contributions to the science of medicine than most men in the past generation—a famous man whom the world loved and respected, and a lovable man who carried his many honors and fame with great modesty.

It was my good fortune to have worked with him when there were but seventeen men on the staff of the Clinic, at a time which afforded us a closer and a more intimate association with him and his distinguished brother than was given to the men who served in the Clinic after the staff had become so large. This very intimate association with him gave us fortunate men a splendid opportunity to become well acquainted with his many outstanding characteristics—his lovable and appealing personality—his keen mind—as well as his surgical brilliance.

He embodied everything that is noble and fine in a great physician. His love for his patients, the gentleness and patience he showed them during busy days when he was driven almost beyond the point of endurance, were outstanding traits. His knowledge of human psychology and his ability to relieve those racked with emotions and fears by his marvelous personality left an indelible imprint upon the minds of all of his associates. His keen analysis of suggestions and of new methods which were continuously being made in the rapid changes which were taking place in medicine at that time and the excellent judgment which he invariably showed in accepting only those methods and suggestions which later proved to be good was a source of wonderment to us all; and his own practical suggestions and the ingenious methods which he originated were legion.

His great versatility in the operating room was well known to all who ever attended his clinics. It was not unusual for him in a morning's work to cover practically the whole body and to explore most of its systems—all of his operations being performed with deftness and with an accuracy made possible by his broad knowledge of the anatomy, the physiology, and the pathology of the part under consideration, and invariably each operation was performed with conservatism, great gentleness, and with the dispatch of a master. As a diagnostician he was

unexcelled, often arriving at his conclusions by an uncanny intuitive sense apprehending obscure conditions unrecognizable by laboratory or mechanical aids.

But the privilege of making rounds with him, of working with him during the afternoon hours in the Clinic, and of spending evenings with him in his home was just as instructive and I believe of as much value as assisting him in the operating room, for here his true greatness was shown in his love for his fellowman, his interest in his patients, in their problems as well as their diseases, his gentle consideration of the poor and unfortunate, his love for facts and his hatred of sham and subterfuge. Continuously in his work he practiced the true art of medicine to the highest degree.

What a brilliant, wonderful man! How wide his interests! Great surgeon though he was, his views were not limited to the medical field but embraced a myriad of subjects to which he brought his keen discernment and understanding. He had a most unusual knowledge of mechanics and this he applied to his work, incorporating many practical and ingenious methods in the operations which he devised and originated. But an outstanding trait that everyone who knew or met him will long remember was his shrewd, dry wit, his delicious sense of humor, and a Will Rogers' way of expressing it. His presentation of deep scientific facts was never in the dry pedantic style, though packed with profound learning and wisdom. He always brought in some bit of homely philosophy, some excruciatingly funny witticism that left his audience breathless with laughter but left his point indelibly etched in their minds.

His home life was ideal. His great love for his devoted and wonderful wife, his children, his distinguished brother, and for his countless numbers of patients and friends was additional evidence of his greatness. Even after fame and world recognition came to him and he was showered with honors that have been given to few men in medicine, he was the same sweet, lovable, modest, and unspoiled Dr. Charlie that he was in the old days before all of these came to him. How few of us are big enough to bear recognition and fame in such a way!

Dear Dr. Charlie—what a heritage you have left and how much your life has benefited and enriched us! To the thousands of your patients who have been relieved and saved by your skill, to the countless numbers of physicians who have profited by your teachings, and to your legion of friends you shall always remain not only an inspiring and a stimulating influence but a sweet and lasting memory especially to your "old boys" who loved you and who will treasure that memory deep in their hearts to the end.

DONALD GUTHRIE.

THE SURGEON'S LIBRARY

REVIEWS OF NEW BOOKS

THE W. B. Saunders Company offers the seventh edition of DeLee's *Principles and Practice of Obstetrics*.[1] In the preface to this edition the author states that 44 pages have been added but these are used chiefly for illustrations. He also states that every page has been worked over and obsolete matter has been omitted. It is a volume of over 1,100 pages which contains 1,277 illustrations.

This seventh edition has the same arrangement as the previous editions and like its predecessors presents a very exhaustive survey of each subject. There is a substitution for some of the illustrations, such as Falkiner's ovum for Herzog's, which was reproduced in the sixth edition. It is noted that the former is included in color in another obstetrical text of recent edition. As in previous editions, the bibliography is given at the end of each chapter rather than one complete bibliography at the end of the volume. It is DeLee's textbook brought up to date.

CHESTER C. DOHERTY.

IN the introduction to the book, *Surgical Treatment of Hand and Forearm Infections*,[2] Dr. T. Wingate Todd has written:

"To both Dr. Brickel and myself it is a matter of the deepest dismay that at the very moment when we should have wished to consult with Dr. Kanavel on this important work Fate has intervened and left us to carry on without his constructive criticism and approval."

No one who knew Dr. Kanavel would doubt that he would have been the first to congratulate the author upon his efforts to extend our knowledge of the anatomy of the hand and the subject of infections, and to express his gratification that other men were taking up the cudgels to help fight a battle which had always seemed to him of such great importance. Furthermore, I think no one would doubt that he would have helped the author to correct some of the interpretations that he has made from his studies.

The first third of this very well illustrated volume is devoted to an anatomical study of the hand and forearm and is profusely illustrated with drawings of anatomical dissections and reproductions of roentgenograms made after injections of opaque materials into various sheaths and spaces. A finding that has impressed the author forcibly is the filling of a large space within the palm as a result of injection of the tendon sheath of the fifth finger (Plates XX–XXII). This he has considered to be the ulnar bursa. He has ignored the fact that the ulnar bursa, or to use a descriptive term, the synovial sheath which invests the flexor tendons in the proximal portion of the palm, except for that portion which continues distally about the flexor tendons of the little finger, ends rather abruptly just distal to the middle of the metacarpus and does not continue distalward about the lumbrical muscles.

In the plates immediately following (XXIII and XXIV) the author shows the ulnar bursa fairly well outlined. The latter roentgenograms were obtained after injection of the exposed proximal end of the bursa. "Both injections were stopped when the material began to leak from the openings previously made at the distal ends of the tendon sheaths of thumb and little finger." Surely if injected material leaked from the distal ends of tendon sheaths of thumb and little finger the ulnar bursa, or the synovial sheath investing the flexor tendons in the palm, should be filled and delineated. As a matter of fact it is; and the picture shown in Plates XXIII and XXIV is very similar to the well known illustration in Kanavel's book (sixth edition, p. 53; seventh edition, p. 48) which shows the tendon sheaths of index, middle and ring fingers, and the radial and ulnar bursæ after injection with a suspension of red lead; and to Best's illustration showing the sheaths after injection with gelatin (Ann. Surg., 1939, 89: 371). However, the injected space shown in Plates XXIII and XXIV has no similarity whatever to those shown in Plates XX–XXII. Why injection at one end of a synovial sac should give one picture and an injection at the other something entirely different is not explained.

The delineation of the synovial sheaths of the index, middle and ring fingers is not clear in any of the plates. In Plates XVIII and XXI, particularly, there has been widespread extravasation into the soft tissues of the fingers as the result of attempted injections into the flexor sheaths. Nowhere is there seen a simple, clear cut picture of the synovial sheaths of index, middle and ring fingers such as shown in the illustration by Kanavel referred to above. There are two possible explanations for this failure: one, that the needle or cannula slipped from the sheath. The result obtained would be comparable to the extravasation that occurs when a needle slips from or through a vein in an attempted intravenous injection. The other possible explanation is that the anatomical material used was so firmly fixed and hardened by chemical preservatives that

[1] THE PRINCIPLES AND PRACTICE OF OBSTETRICS. By Joseph B. DeLee, A.M., M.D. 7th ed. Philadelphia and London: W. B. Saunders Co., 1938.

[2] SURGICAL TREATMENT OF HAND AND FOREARM INFECTIONS. By A. C. J. Brickel, A.B., M.D. St. Louis: The C. V. Mosby Co., 1939.

no injection of synovial sheaths in the fingers was possible. Anyone who has attempted only to straighten the flexed fingers of extremities "long pickled in brine" can appreciate how difficult it might be to demonstrate by injection the synovial sheaths in such a hand.

Since the tendon sheaths of index, middle or ring fingers were not filled with the injected material it is obvious why they did not rupture into the middle palmar space or thenar space, as was demonstrated so graphically by Kanavel in his experimental studies and as has been demonstrated so often in a multitude of clinical cases. Injected material did rupture from the tendon sheath of the fifth finger into the palm and give the outline of the middle palmar space shown in Plates XX–XXII, and incorrectly called the ulnar bursa. Interestingly enough such rupture almost never occurs as a result of infection within the tendon sheath of this finger. We have seen many cases in which infection extended from the little finger into the ulnar bursa and forearm, but not a single case in which it ruptured from the sheath of the fifth finger into the palm. This fact again suggests the importance of checking by other methods conclusions drawn from experimental injections of anatomical material which may have been firmly fixed by chemical preservatives. These illustrations (Plates XX–XXII) do show graphically that material injected into the middle palmar space can pass lateralward beyond the middle metacarpal bone if no median septum is present to limit its spread, if the septum is ruptured or if it is displaced (flattened) radialward and dorsalward by the injected material. This was emphasized by Iselin,[1] and his illustration of the injected "deep middle palmar space" (espace palmaire median profond) is identical with that shown in the author's Plates XX and XXI.

The author ignores the fact that Kanavel demonstrated that injected material which ruptures from the overdistended tendon sheath of the index finger fills the thenar space. Dr. Brickel has pictured a space (Plate XXX) which he calls the adductor space (a good name), resulting from injection of opaque material "at the distal edge of the thumb web . . . the shadow of the main mass of injected material lies to the radial side of the third metacarpal bone corresponding to what some authors call the thenar space. . . . Subsequent dissection of the hand showed that the material was confined to the fascia and body of the adductor pollicis."

In spite of the fact that the author points out that the mass lies to the radial side of the metacarpal bone and that the illustration, as well as the following plate (XXXI) show this definite line of demarcation he states elsewhere: ". . . we have never found a special palmar septum dividing the palmar foyer into halves" (p. 98) and, "We have never seen in our dissections or injection experiments a septum in the palm running from the palmar fascia to the middle metacarpal bone. In support of this observation an independent dissection was made for the author during the summer of 1937 by Dr. Schmeidel, Professor of Anatomy at the University of Vienna" (pp. 158–159). How the injected material shown in Plates XXX and XXXI (the form assumed by the injected material and its position are identical in the two figures) remains confined to the area radial to the third metacarpal bone if there is "no septum dividing the palmar foyer" is not explained.

The last two-thirds of the volume are devoted to a discussion of various types of infection and their treatment. In the discussion of general principles there are many statements with which we would wholeheartedly agree, "Local anesthetics have definite drawbacks. . . . Encircling injections into the base of the finger with the application of a tourniquet to hold in the anesthetic is dangerous because gangrene of a finger may result. Injections of local anesthetics into the finger tip are especially to be avoided because distention of the tissues is very painful and likely to cause necrosis." "Ethyl chloride spray as a local anesthetic has nothing to commend it. . . . We do not favor local injections, block or brachial anesthesia."

No mention is made of the invaluable blood pressure band to secure a bloodless field during operation, and little attention is given the importance of careful and complete immobilization as a part of the after-care, or of methods of securing immobilization; and to the important principles of simple surgical cleanliness—of aseptic care of infected hands in the days following separation.

In a discussion of infections of the finger tip it is stated, "An abscess in the bone must be curetted. . . . If no surgical attempt is made to eradicate the sequestrum a long period of distress and disability is certain to follow" (p. 115). "Where the bone is affected superficial abscesses may be curetted and the site of the abscess cauterized with carbolic acid and washed off with alcohol or glycerin. *Care must be taken to limit the necrosis resulting from use of phenol*" (p. 134); and in a discussion entitled "Infections of the Bones and Joints" one reads, "To curette infected areas in the bone is unwise; it is hard to know how much of the bone is actually diseased because soft, mushy, demineralized bone is present in the immediate vicinity of the infected bone. It is much better to provide adequate drainage and to await the formation of sequestra."

With the last of these three statements we would agree completely, but in the face of such conflicting statements how will the "seeker after knowledge" be able to choose the proper treatment? Surely there is no difference in the treatment of bone infection in the distal phalanx and in a metacarpal or carpal bone; and it is difficult to see any difference between the use of phenol with its resulting necrosis and the boiling oil which Paré abandoned so long ago.

The author has devoted a considerable portion of the space available for clinical considerations to the simple infections. In this he has doubtless chosen wisely, for the simple infections are the common

[1]Surgery of the Hand. Masson & Co., 1933, Fig. 55, P. 158.

ones. The various types of local infection are well described and well portrayed. One case described as a palmar abscess (Figs. 54–57) has all the characteristics of an infection of the thenar space, which may have gone on to rupture into the middle palmar space. It would be difficult to distinguish it from the case pictured in Figures 96 and 97 as a thenar space abscess.

Some of the very complete case reports arouse the "deep dismay" that Dr. Todd has mentioned in his introduction: dismay at the radical surgical procedures that are sometimes carried out in the face of an acute and rapidly spreading infection (pp. 125–131); and at the many and extensive operative procedures of an exploratory nature to which patients are subjected when the surgeon has failed to make an exact diagnosis (pp. 244–253).

The writer of this review cannot hope to bring to a consideration of the problems involved in this book the judgment and discrimination that Dr. Kanavel would have brought as a result of his many years of careful observation and wide experience. He cannot help but regret that the author did not seize the opportunity (the Introduction states "It is now many years since I asked Dr. Brickel to undertake a special study of the hand, etc.") to discuss these problems with Dr. Kanavel while the opportunity was still present. SUMNER L. KOCH.

THE revival of an old classic is presented in the centennial edition of Franz Carl Naegele's *Obliquely Contracted Pelvis*[1] edited by Hellman and Musa. Naegele's original, published in 1839, contained 120 pages of text and 16 lithograph plates in 2 colors. There was a French translation in 1840 and an English translation in 1848, but according to the editors of this edition neither of these was complete as written by Naegele. The original text is practically unobtainable; however, one of the editors owns a copy purchased in Berlin in 1914 from which this translation was made, to quote the editors, "It will for the first time make the original text available in English, together with the lithographs of the original edition again produced by lithography in 2 colors." A short sketch of Naegele's academic life is included in the preface.

In his introduction to this work Naegele gives his reasons for publishing it in the form of a monograph: "It permits of wider distribution and is more likely to attract the attention of the scientific world than journal contributions." He recognized the erroneous conceptions that would be obtained by conclusions drawn from superficial examinations and the observance of a few cases. He furthermore recognized the existence of literary pirates who were ever on the alert, ready to pilfer the work of industrious individuals and call it their own, after some attempt at disguise. The similes he applies to such practice are noteworthy.

The first 2 specimens of the type of deformed pelvis described in this treatise were observed by the author in 1803. Another was observed 10 years later and again one was observed in 1838. Naegele deduced that these rare and peculiar deformities of the pelvis and their striking similarity were results of a common basic cause and urged his colleagues to be on the lookout for such specimens. In 1832, he introduced these pelves as a "new special pelvic deformity" at a meeting of the Society of Natural Science and Medicine. He considered this type of pelvis just as important as other pathological types and continued to exhort his colleagues to look for them.

These pelves all resemble one another, the only difference being the degree of distortion. The condition of the bone otherwise is normal. There is no evidence of rickets or osteomalacia. Neither history nor evidence of previous injury is present. There is no limping in these cases, but the lumbar vertebræ are rotated somewhat toward the ankylosed side. Thirty-five female and two male pelves of this variety are described in detail and due credit is given the finder of each. Three female pelves are described which resemble the obliquely contracted pelvis, except that the synchondroses are normal. A male pelvis in which the fusion of the ileum and sacrum is complete but which lacks the unilateral atrophy of the os sacrum is described.

In commenting on the frequency of this type of pelvis, Naegele states that he believes it occurs "not infrequently," but for obvious reasons they are not discovered. He believes that the condition originates from a deviation in development and that disease has no part in the etiology. He outlines his reasons for this belief and they are logical. The effect of this deformity on labor is discussed and the difficulty of its diagnosis is stressed.

Five tables giving differences in various dimensions on 8 of the pelves described show the constancy of this inequality of the 2 sides. There follows a description of pelvic contractions of severe degree and comments on the differential diagnosis between rickets and osteomalacia.

Sixteen lithograph plates which represent some of the 35 pelves described by Naegele complete this unique volume.

Naegele disagreed with the dogmatism of some of his colleagues and contemporaries and calls attention to the dangers which may be involved in following such aphorisms.

The editors are to be congratulated for making available to the profession this work of which so few copies of the original are extant. Practically nothing has been added to the knowledge of this subject in the elapsed hundred years since its publication by Naegele, except perhaps that it is possible to diagnose the condition by the aid of roentgenography rather than at the autopsy table.

CHESTER C. DOHERTY.

[1] THE OBLIQUELY CONTRACTED PELVIS; CONTAINING ALSO AN APPENDIX OF THE MOST IMPORTANT DEFECTS OF THE FEMALE PELVIS. By Franz Carl Naegele. Mainz: Victor von Zabern, 1839. Centennial Edition, Newly Translated from the Original German by Alfred M. Hellman, M.D., F.A.C.S., and George Musa, M.D. New York: Pynson Printers, Inc., 1939.

THE book, *Surgery of Oral and Facial Diseases and Malformations*,[1] represents a compilation entailing an earnest effort to condense the meat of a tremendous field into a reasonable volume. In the main, the book fulfills the requirements of a textbook, in that it is authentic and presents the subject matter in acceptable form, readable, and profusely illustrated. The illustrations are good with the exception of the roentgenograms and some of the line drawings; these do not adequately illustrate the author's own operations.

The arrangement of the text is unusual. Opening with a chapter on anesthesia, hemorrhage, blood transfusion and shock, the outline plan is extended along familiar lines. The chapter dealing with diseases of the nervous system is acceptable and rarely found in a book of this kind. The vexed subject of focal infection of oral origin is dealt with in a common sense manner, and food for thought is provided the specialists in orthodontia.

Consideration of plastic surgery as a specialty is taken up in a readable form, and the author presents procedures adopted by himself and those in authority in a manner designed to make the book a useful reference volume.

The book cannot be recommended wholeheartedly as a textbook for dental students, because they are concerned particularly with essentials and not with major surgical procedures for which they are not trained. On the other hand, as a guide to dental and medical practitioners and surgeons, the book may be read with profit. F. W. MERRIFIELD.

[1] THE SURGERY OF ORAL ANT FACIAL DISEASES AND MALFORMATIONS; THEIR DIAGNOSIS AND TREATMENT, INCLUDING PLASTIC SURGICAL RECONSTRUCTION. By George Van Ingen Brown, D.D.S., M.D., C.M., F.A.C.S. 4th rev. ed. Philadelphia: Lea & Febiger, 1938.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

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CLINICAL PATHOLOGICAL GYNECOLOGY. By J. Thornwell Witherspoon, B.S., B.A. and M.A.(Oxon), M.D. Philadelphia: Lea & Febiger, 1939.

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CIRURGIA DO MEGAESÔFAGO. By Edmundo Vasconcelos and Gabriel Botelho. Sao Paulo, Brazil: Companhia Editora Nacional, 1937.

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CORRESPONDENCE

THE AMERICAN CONGRESS ON OBSTETRICS AND GYNECOLOGY

PREPARATIONS are being rapidly completed for the first American Congress on Obstetrics and Gynecology to be held in Cleveland the week of September 11, 1939. This meeting should be extremely profitable to everyone who has any interest in gynecology or maternal and infant care. This American Congress was planned to provide an opportunity to study and to correlate all the many problems in these special fields. Such a meeting was suggested by the Central Association of Obstetricians and Gynecologists. Its planning and successful organization has been carried out by the American Committee on Maternal Welfare, with Dr. Fred L. Adair, of Chicago, as chairman. It has had the active support of national and local organizations interested in this work. The following societies have contributed active workers and financial aid: American College of Surgeons, American Association of Obstetricians, Gynecologists and Abdominal Surgeons, American Gynecological Society, American Hospital Association, American Medical Association, Section on Obstetrics and Gynecology, American Medical Women's Association, American Nurses Association, American Protestant Hospital Association, American Public Health Association, Catholic Hospital Association, Central Association of Obstetricians and Gynecologists, Chicago Maternity Center, Maternity Center Association of New York, National League of Nursing Education, National Medical Association, National Organization of Public Health Nursing, New England Obstetrical and Gynecological Society, Pacific Coast Society of Obstetrics and Gynecology, Southern Medical Association, U. S. Bureau of the Census, U. S. Children's Bureau, U. S. Public Health Service, Chicago Gynecological Society, Detroit Obstetrical Society, Illinois State Nurses Association, Minnesota Obstetrical and Gynecological Society, New Orleans Gynecological and Obstetrical Society, New York Obstetrical Society, Pittsburgh Obstetrical and Gynecological Society, Texas Association of Gynecologists and Obstetricians, and the Obstetrical Society of Boston.

The Congress will afford the first opportunity to all the professional personnel interested in the problems of obstetrics and gynecology to meet together for a discussion of the various phases of maternal and infant care and to correlate these problems. To this end doctors, nurses, public health workers, and hospital administrators and educational leaders are invited to participate. These separate groups have arranged unusually comprehensive programs in their own special fields and have integrated their problems with those of the other groups.

The general plans of the meetings will provide separate morning sessions for doctors, nurses, and public health workers. Noonday round table discussions will provide an opportunity for more informal consideration of important subjects. The afternoon meetings will bring together all of the members of the Congress in programs of general interest to the entire group. Evening meetings will be of general interest and will be broadcast; outstanding individuals outside of the field of medicine will present the social implications of the problems of reproduction to the Congress.

The medical program will include round tables and discussions of obstetrical and gynecological subjects by leading specialists. Monday morning will be devoted to medical and surgical complications of pregnancy, Tuesday morning to gynecological complications, Wednesday morning to the problems of labor. Endocrinology in obstetrics and gynecology, including the subject of sterility, will be presented Thursday, and Friday morning will be given over to a discussion of infection in obstetrics and gynecology. A round table discussion will be offered every day on each of the following subjects: Toxemias of pregnancy, genital infections, obstetrical and gynecological hemorrhages, the fetus and the newborn, anesthesia, analgesia and amnesia in labor. These subjects will be repeated daily under the chairmanship of a clinician who has made outstanding contributions on the subject. This will therefore give an opportunity to a maximum number of individuals to attend these round table discussions.

The section on public health will present a similar program. The subjects to be covered in the morning meetings are the following: Public health and maternity care, maternal care in the

rural areas, federal and state programs in maternal care, maternal care and economics, education and maternal care. The afternoon meetings of component groups attending the Congress will correlate all the subjects which have been considered at the morning meetings of special groups.

The scientific exhibit which is to be held in conjunction with the Congress will be unusually comprehensive. New developments in obstetrics and gynecology will be presented and illustrated by diagrams, pictures, models, and moving pictures. Although investigations underway in the large teaching centers will predominate in this exhibit, some of the exhibits will have a wider scope in that they will attempt to portray the relationship of the problems of reproduction to the profession and to the general public.

The Congress should stimulate the development of state and local programs for better care for mothers and babies. It should likewise direct public attention favorably toward these problems and their successful solution by the profession. Thus, it should prove to be a force for tremendous good in bringing the public and profession together in the best interests of both.

In order to achieve the greatest good the Congress must have a wide representation. The entire medical profession is cordially invited to membership. The general practitioner, in particular, is urged to attend for he will find the meetings will provide him with a week's intensive instruction in all the phases of obstetrics and gynecology. Nurses and hospital administrators should likewise be urged by their medical staffs to attend.

The nominal registration fee of $5.00 includes a year's membership in the American Committee on Maternal Welfare. All interested individuals are urged to send in their registrations in the American Congress on Obstetrics and Gynecology to the headquarters' office, 650 Rush Street, Chicago, Illinois. Checks should be made payable to Dr. R. W. Holmes, Treasurer. A detailed program of the meetings and scientific exhibits will be mailed on request.

M. EDWARD DAVIS, M.D.

A NEW AND SAFER METHOD OF CITRATED BLOOD TRANSFUSION

THE statement in a paper entitled "A New and Safer Method of Citrated Blood Transfusion" by Hustin and Dumont that "one of them (Hustin) advocated the citrate method for the first time 25 years ago" requires correction.

Hustin (April, 1914) used sodium citrate in blood transfusion, but in order to prevent coagulation he felt it was necessary to mix the blood with an equal volume of glucose solution. Thus as Hédon (1917) stated, "Hustin mixed in equal parts blood with isotonic glucose salt solution, containing a certain proportion of sodium citrate and injected this mixture in small quantities. Hustin's method of transfusion is really an infusion of strongly diluted blood mixed with citrate of soda and glucose."

It was only after Agote and I (January, 1915), working independently and contemporaneously, showed that undiluted citrated blood could be used for blood transfusion that the method had any practical value. This statement of facts shows ve ry definitely that Hustin cannot be justly considered as the author of the citrate method. Questions of priority are of minor importance, but questions of technique interest not only those who have helped in the development of a new method, but are of great importance to the profession at large. For this reason the fact that Hustin and Dumont claim to present a "safer" method of citrated blood transfusion requires careful investigation.

At Mount Sinai Hospital and in most hospitals in this country the technique which I described nearly 25 years ago is still used today with one important modification. Instead of the original piece of glass tube, a connecting piece with a dropper is used in order to employ the intravenous drip method for blood transfusion. The intravenous drip method of infusion was first used by Friedemann over 25 years ago. The provision for Friedemann's continuous intravenous drip is the only important change which we have made in the original apparatus for citrate transfusion in 25 years.

The method as we have used it at this Hospital since 1915 represents an open method. Ever since its introduction in 1915, attempts have been made by others to introduce closed methods. People thought that the frequency of chills which were formerly encountered following citrate transfusions might be due to infection through the air. Naturally all closed methods are much more complicated than the open method which consists of a glass jar and an infusion flask. Since Rosenthal showed that chills are due to foreign proteins and to defects in the distillation of the water, closed methods have practically been abandoned. Rosenthal showed that careful cleansing of the instruments, tubing, and glassware immediately after the transfusion is essential for the prevention of chills. Since this technique was introduced at Mount Sinai Hospital in 1932 the chills dropped from 12 per cent to 1 per cent and have stayed on that level ever since. In 1937, 1699 citrate transfusions were given in the wards of Mount Sinai Hospital.

Hustin and Dumont have devised a new apparatus (closed method) to which they add a propelling machine on the Carrel principle. The fact that with this complicated apparatus the incidence of chills was three times as high as with the open method will naturally stand in the way of its popularization.

RICHARD LEWISOHN, M.D.

CLINICAL CONGRESS OF AMERICAN COLLEGE OF SURGEONS

HOWARD C. NAFFZIGER, San Francisco, *President*
GEORGE P. MULLER, Philadelphia, *President-Elect*

Committee on Arrangements
THOMAS A. SHALLOW, *Chairman;* L. KRAEER FERGUSON, *Secretary*

PLANS FOR 1939 CLINICAL CONGRESS IN PHILADELPHIA

FOR the twenty-ninth annual Clinical Congress of the American College of Surgeons, the surgeons of Philadelphia are planning to present a program of operative clinics and demonstrations that will include all phases of their clinical activities in this great medical center.

During the five days, October 16–20, the clinicians at the five medical schools and more than 40 hospitals participating in the program will demonstrate to the fellows and their guests the latest advances in surgical technique and operative procedures. A preliminary schedule of the clinics and demonstrations at the hospitals and medical schools was published in the June issue of this journal and will be republished in later issues as the program is revised and amplified during the months preceding the Congress. Clinics will be held on the afternoon of Monday, October 16, and the mornings and afternoons of each of the following four days.

The program presents an ample and well arranged schedule of operative clinics, at which the technique of a wide variety of surgical procedures will be demonstrated. In addition, the committee is arranging a series of non-operative clinics in many of the large hospitals for the presentation of important work being done in many special fields. Demonstrations and exhibits will cover many phases in general surgery, genito-urinary surgery, neurosurgery, obstetrics and gynecology, fractures and other traumas, surgery of the bones and joints, thoracic surgery, broncho-esophagology, plastic and faciomaxillary surgery, and surgery of the eye, ear, nose, and throat. The hospital schedules will be so correlated that the visiting surgeon will be assured of an opportunity to devote his time continuously, if he so desires, to clinics dealing with the special subject in which he is most interested. In the final program the clinical schedules will be classified according to various specialties in order to aid the visiting surgeon in selecting the clinics which he desires to attend. An accurate, detailed clinical program will be posted in the form of bulletins at headquarters each afternoon, for the succeeding day, and published in printed form for distribution each morning.

The annual meeting of the governors and fellows of the College will be held in the Rose Garden of the Bellevue-Stratford Hotel on Thursday afternoon at 1:30 o'clock. Reports on activities of the College will be presented by the officers and chairmen of the standing committees.

The meetings of three important state and provincial committees are to be held on Wednesday forenoon in the Palm Garden on the first floor of the hotel as follows: Judiciary committees, 9:30; Credentials committees, 10; Executive committees, 11.

As the showing of surgical motion picture films so faithfully depicts clinical features of major interest to surgeons, it is planned to present at this year's Congress an enlarged program of both sound and silent pictures at daily exhibits in the Palm Garden of the headquarters hotel.

SCIENTIFIC SESSIONS

The scientific sessions will include certain new features introduced at the Congress in recent years which have met with desired success. The schedule of midday panel discussions has been greatly extended in order that a larger number of the visiting surgeons may have an opportunity to participate.

On Monday the initiates will assemble in the Palm Garden at 11 a.m. in order that the officials

of the College may meet them and explain in some detail the aims and objectives of the program of the College. At this same session, the fellowship roll will be signed by the initiates. In the evening, at the Academy of Music, the Presidential Meeting and Convocation will be combined and at this time the new officers inaugurated and the initiates received into fellowship. Dr. Howard C. Naffziger, of San Francisco, will deliver the presidential address, and distinguished surgeons from foreign countries will be introduced.

Scientific meetings will be held in Irvine Hall of the University of Pennsylvania on Tuesday, Wednesday and Thursday evenings, at which eminent surgeons of the United States and Canada, with the co-operation of internists, will present various phases of the interesting subjects which have been selected for discussion.

As in former years, afternoon symposia have been arranged on the subjects of cancer, fractures and other traumas, urology, obstetrics and gynecology, and thoracic surgery.

A special feature of the program includes a series of clinical demonstrations to be held at headquarters each morning for those visitors interested in the subjects of ophthalmology and otorhinolaryngology. The subcommittees in charge of these special arrangements are also planning extensive programs of operative and dry clinics in surgery of the eye, ear, nose, and throat to be held in the hospitals each afternoon. Programs for special evening sessions of these groups are being prepared for Tuesday and Thursday evenings.

The midday panel discussions have become of such major interest as a feature of the Congress that the series for this year's meeting will include fifteen such sessions in large well-lighted rooms. The program will permit the formal and informal discussion of subjects in more restricted fields than would be susceptible of treatment in the general meetings. Attendance at these conferences will necessarily be restricted to the capacity of the rooms in which they will be held. Outstanding authorities have co-operated with the College in the presentation of each one of the selected subjects and will lead, direct and participate in these discussions. The general plan to be followed is that the leader will present the subject to be discussed within a ten minute period, and selected men will discuss various phases of these topics briefly after which general discussion from the floor will be encouraged.

The program committee has aimed to include a selection of material at these various scientific meetings which will make it possible for all of the general surgeons and surgical specialists attending the Congress to learn of the newer developments in their respective specialties.

GRADUATE TRAINING FOR SURGERY

Following the annual meeting of the fellows on Thursday afternoon, a conference on graduate training for surgery will be held in the Ballroom at 3:00 p.m. Raising the standards of surgery has been a primary purpose of the American College of Surgeons since its organization. This will be accomplished through the present program of the College which has stimulated added interest in this subject on the part of all its fellows and a large number of approved hospitals. The Committee on Graduate Training for Surgery will present its report of activities for the year through its chairman, Dr. Dallas B. Phemister, of Chicago. Also, at this time, the list of hospitals approved for graduate training for surgery in the United States and Canada will be announced. Leaders in the field of graduate medical education will present and discuss at length the various phases and problems of organization and conduct of graduate training for surgery. This session should be of vital interest to the entire fellowship of the College and many practical suggestions will be offered for developing the needed systematic supervision, preceptorship, and guided instruction for young surgeons.

HOSPITAL CONFERENCES

The twenty-first annual Hospital Standardization Conference will open the Clinical Congress with a session in the Rose Garden at the Bellevue-Stratford Hotel on Monday morning at 10 o'clock. Official announcement of the approved list of hospitals for 1939 will be made at this session.

On Monday afternoon, and on Tuesday, Wednesday and Thursday, both morning and afternoon, an interesting program of papers, round table conferences and practical demonstrations, all dealing with various problems related to efficiency in the hospital, will be presented. On Wednesday and Thursday afternoons, at certain local hospitals, demonstrations in administrative and technical procedures will be conducted which will be of great interest to the hospital visitors.

At the hospital conference on Tuesday afternoon there will be an administrative panel round table discussion in which an effort will be made to cover as many aspects of hospital administration as possible with particular emphasis on maintenance of high professional standards, current economic problems and trends, and other timely subjects.

A special feature of the hospital conference will be a meeting of hospital executives on Tuesday evening when the program will deal with the future of the voluntary hospital, training of hospital administrators, etc.

At a joint session with the Association of Medical Record Librarians of North America on Wednesday morning the subject of medical records will be considered from the standpoints of the various specialties of medicine and surgery.

There will be ample opportunity during the Congress for the visitors to inspect the hospitals in Philadelphia and vicinity.

HEADQUARTERS—TECHNICAL EXHIBITION

Headquarters for the Congress will be established at the Bellevue-Stratford Hotel where there are unusual facilities for accommodating the Congress. The Grand Ballroom, Garden, Clover and Red rooms and other large rooms on the first and second floors and the roof have been reserved for scientific exhibits and conferences, registration, clinic ticket bureaus, bulletin boards, executive offices, etc. Thus, the activities of the Congress will be centralized under one roof.

The technical exhibition will be located in the Ballroom and adjacent rooms on the second floor. The registration and clinic ticket bureaus, together with the registration desk, will be centrally located on that floor. The bulletin boards, on which the daily clinical programs will be posted each afternoon, will be distributed through the exhibit rooms. Leading manufacturers of surgical instruments and supplies, x-ray equipment, operating room lights, hospital apparatus of all kinds, ligatures, dressings, pharmaceuticals, and publishers of medical books will be represented in the exhibition.

ADVANCE REGISTRATION

The hospitals and medical schools of the Philadelphia area afford accommodations for large numbers of visiting surgeons, but to insure against overcrowding, attendance at the Congress will be limited to the number that can be comfortably accommodated at the clinics. The limit of attendance will be based upon the results of a survey of the operating rooms and laboratories of the hospitals and medical schools to determine their capacity for visitors. It is expected, therefore, that those surgeons who wish to attend the Congress will register in advance. A registration fee will be required in order to provide funds with which to meet the expenses of the Congress. A formal receipt will be issued to each surgeon registering in advance which is to be exchanged for a general admission card upon his registration at headquarters during the Congress. This card, which is not transferable, must be presented in order to secure clinic tickets and admission to scientific sessions.

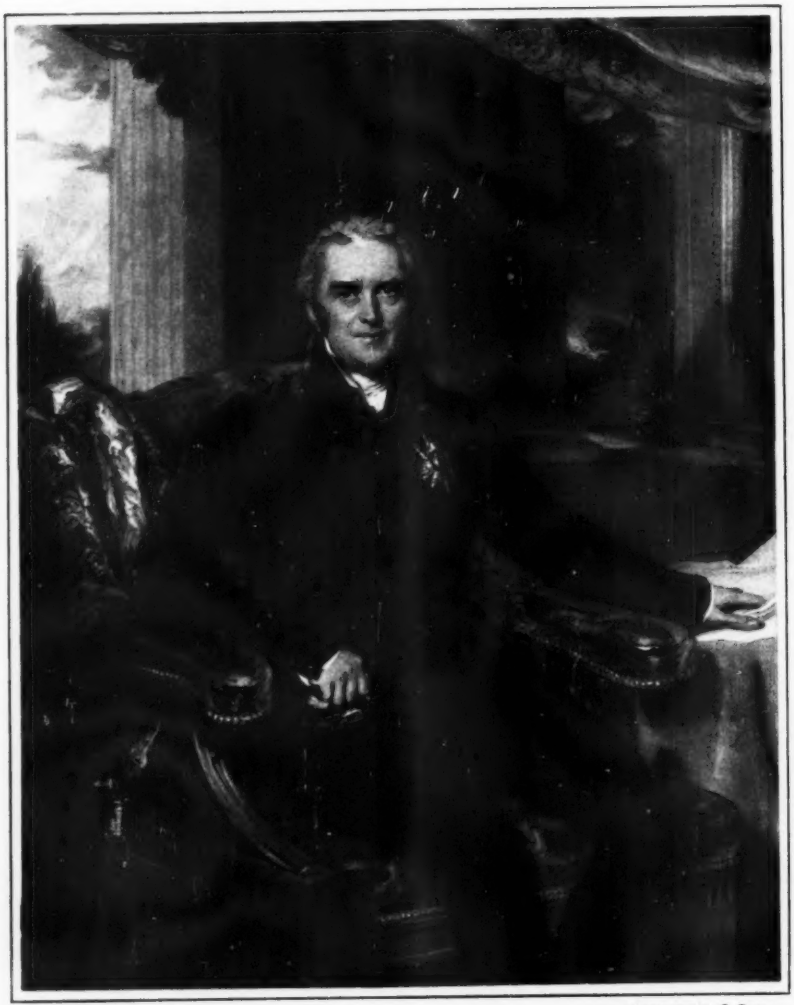
A resolution adopted by the Board of Regents provides that the registration fee for fellows and endorsed junior candidates shall be $5.00; that no fee for the 1939 Congress shall be required of initiates (class of 1939); that the fee for non-fellows attending as invited guests of the College will be $10.00.

As in previous years, admission to clinics and demonstrations at the hospitals will be controlled by means of clinic tickets, which plan provides an efficient means for the distribution of visiting surgeons at the various clinics and assures against overcrowding. The number of tickets issued for any clinic will be limited to the capacity of the room in which the presentation is held.

PHILADELPHIA HOTELS AND THEIR RATES

In addition to the headquarters hotel, the Bellevue-Stratford, there are many first-class hotels within a short walking distance, providing ample hotel facilities at reasonable rates. It is suggested that reservation of hotel accommodations be made at an early date at the following hotels which are recommended by the committee:

	Minimum rate with bath	
	Single	Double
Adelphia, 13th and Chestnut Sts.	$3.85	$5.50
Barclay, Rittenhouse Square, E.	4.50	7.00
Bellevue-Stratford, Broad and Walnut Sts.	3.85	5.50
Benjamin Franklin, 9th and Chestnut Sts.	3.85	5.50
Colonial, 11th and Spruce Sts.	2.50	3.85
Drake, 1512 Spruce St.	4.00	6.00
Majestic, Broad St. and Girard Ave.	2.50	4.00
Philadelphian, 39th and Chestnut Sts.	2.75	4.40
Ritz Carlton, Broad and Walnut Sts.	3.50	6.00
Robert Morris, 17th and Arch Sts.	2.50	3.50
Spruce, 13th and Spruce Sts.	1.50	2.50
St. James, 13th and Walnut Sts.	2.75	4.50
Sylvania, Juniper and Locust Sts.	3.00	5.00
Walton, Broad and Locust Sts.	2.50	4.00
Warwick, 17th and Locust Sts.	4.50	7.00
Wellington, 19th and Walnut Sts.	4.00	6.00



Painting by Sir Thomas Lawrence

Engraving by C. Turner

Sir Henry Halford, Bart.

1766-1844